Neurocoeliac disease: Prevalence, diagnosis, treatment and follow up

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

Summary

ID

NL-OMON47970

Source
ToetsingOnline

Brief title
Neurocoeliac disease

Condition

- Gastrointestinal conditions NEC
- Autoimmune disorders
- Movement disorders (incl parkinsonism)

Synonym
Gluten ataxia, neurocoeliac disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Het VUmc innovatie fonds en het VUmc fonds

Intervention

Keyword: Ataxia, Coeliac disease, Gluten, Neurology

Outcome measures

Primary outcome

The main study endpoint will be the prevalence of (neuro)coeliac disease related antibody titres in the neurology cohorts, together with the HLA-DQ type and the Marsh classification based on a gastroduodenal biopsy (only if a biopsy has been performed as standard care).

Secondary outcome

Secondary endpoints will be the effect of a gluten-free diet on antibody titres, neurological symptoms, quality of life and MRI and MR spectroscopy results in patients suspected of gluten ataxia.

Study description

Background summary

Coeliac disease is an immune mediated, chronic inflammatory enteropathy caused by gluten ingestion in genetically susceptible individuals. It is a common disease in Western Europe, with an estimated prevalence of 0.5-1.0%. (Altobelli, Paduano, Petrocelli, & Di Orio, 2014; Gujral, Freeman, & Thomson, 2012) Neurological symptoms have been reported in 8 up to 50% of the patients with coeliac disease, with cerebellar ataxia and peripheral neuropathy being most common. (Burk et al., 2001; Cicarelli et al., 2003) A high prevalence of coeliac disease related antibodies has been found in ataxia patients. (Hadjivassiliou et al., 2013) Autopsy performed on a gluten ataxia patient revealed loss of Purkinje cells throughout the cerebellar cortex, loss of white matter, astrocytic gliosis and microglial activation. T-cell infiltration was seen intra-parenchymal and perivascular, mainly dominated by CD8 positive lymphocytes. (Hadjivassiliou et al., 1998; Mittelbronn et al., 2010) Currently no data on patients with coeliac disease and related neurological symptoms is gathered or stocked in the Netherlands. In this study we will approach this disease as neurocoeliac disease, defined as a neurological illness otherwise

idiopathic in patients with coeliac disease or gluten sensitivity, which stabilizes or ameliorates on a gluten-free diet.

Study objective

The primary (research) objective of this project is to determine the magnitude of the disease burden of neurocoeliac disease in the Netherlands by studying the prevalence of coeliac disease or gluten sensitivity in ataxia patients. The secondary objective is to attain a better understanding of this disease entity by studying and examining different diagnostic tools and studying the effects of a gluten-free diet in a cohort of patients with sporadic ataxia and coeliac disease or gluten sensitivity. We hypothesize that coeliac disease markers (e.g. Transglutaminase 2 and gliadin antibodies) and Transglutaminase 6 antibodies, a proclaimed neurocoeliac disease marker, will be helpful in diagnosing gluten ataxia, a form of neurocoeliac disease and monitoring the effect of a gluten-free diet.

Study design

This a prospective and partly retrospective longitudinal cohort study. We will recruit patients with an unexplained ataxia and test them for coeliac disease or gluten sensitivity, a gluten-free diet will be initiated if necessary, and we will perform follow up for 12 months. During visits, blood will be analysed for antibody titres. If there is no bloodsample yet, a venipunture will be performed for this study specifically. This will also be the case after 12 months. Patients will undergo a magnetic resonance spectroscopy following a magnetic resonance imaging (MRI) scan if the latter is planned for standard care.

Study burden and risks

The risk of participation is considered to be very low to non-existent. This study is mainly observational. What will be extra: possibly extra blood will be drawn if no previous bloodsamples are available or if no venipunctures are performed for standard care. A patient will undergo an MR spectroscopy directly after a standard care MRI which will lead to 8 minutes of extra scan time. The patient will be asked to fill in a brief questionnaire on the quality of life three times.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- * 18 years of age
- Given informed consent
- unexplained ataxia
- Group specific:
o For gluten sensitivity group: at least positive serology or borderline positive serology
o For coeliac disease group: positive serology and positive biopsy results

Exclusion criteria

- No informed consent
- Insufficient knowledge of Dutch language and/or inability to understand the information provided.
- A known and verified cause of the neurological illness
- For MRI specific: Because of the high magnetic field of the MRI scanner, individuals with pacemakers, metallic implants, pregnancy, or certain other conditions (for example a bodyweight over a 140kg) should be excluded unless

they are cleared by a clinical radiologist/physiologist.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-08-2019
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	26-04-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-11-2019
Application type:	Amendment
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	NL67225.029.18