The role of humoral autoimmunity in the aetiology of achalasia.

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Primary:To investigate the presence of disease-specific antimyenteric antibodies and to identify their target-antigen in patients with achalasia.Secondary:- To determine to what extent humoral autoimmunity is the etiological factor in idiopathic...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Observational invasive

Summary

ID

NL-OMON37385

Source
ToetsingOnline

Brief title
Antibodies in achalasia.

Condition

- Gastrointestinal motility and defaecation conditions
- Autoimmune disorders
- Neuromuscular disorders

Synonym
Achalasia, Oesophageal motility disorder

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Achalasia, Aetiology, Antimyenteric auto-antibodies, Humoral autoimmunity

Outcome measures

Primary outcome

Difference in the presence of antimyenteric neuronal antibodies in patients

with achalasia and controls.

Secondary outcome

- Identify the targeted antigen(s) of the antimyenteric neuronal antibodies.

- General quality of life

- Quality of life related to achalasia

- Eckhardt clinical symptom score

Study description

Background summary

Achalasia is rare motility disorder of the oesophagus and characterised by aperistalsis of the oesophageal body and dysrelaxation of the lower oesophagus sphincter (LOS) caused by progressive destruction and degeneration of the neurons in the myenteric plexus. The pathogenesis of the disease is still largely unknown. Genetic, infectious and neurodegenerative mechanisms have been suggested as possible aetiological factors. A better understanding of the aetiological mechanisms of the disease may provide a serological biomarker that can be used as a diagnostic tool and perhaps will allow us to identify the disease in an earlier stage before widespread destruction of the neurones has occured.

A causative role for autoimmune mechanisms in achalasia gained more support in the recent years due to the association of achalasia with other autoimmune diseases and histopathology of the oesophagus of patients with achalasia which showed activated lymphocyte infiltrates within the myenteric plexus. Furthermore it has been suggested that antimyenteric antibodies play an important role in this disease because various studies have observed antineuronal antibodies in the serum of patients with achalasia. None of these

studies however, reported that the antineuronal anitbodies are specific for a single subtype of the enteric neurones in the myenteric plexus, while it is suggested that in achalasia especially inhibitory neurones are decreased. This brings in to question if the antimyenteric antibodies are pathogenic for achalasia or just an epiphenomenon. Clearly a better understanding of the actual role of humoral autoimmunity in patients with achalasia is needed.

Study objective

Primary:
To investigate the presence of disease-specific antimyenteric antibodies and to identify their target-antigen in patients with achalasia.

Secondary:
- To determine to what extent humoral autoimmunity is the etiological factor in idiopathic achalasia.
- To investigate whether antineuronal antibodies can be used as a biomarker of achalasia.
- To find new targets for therapy focused on humoral autoimmunity.
- Collect demographic and clinical data of patients with idiopathic achalasia and first degree relatives.

Study design

A prospective observational study

Study burden and risks

Patients with achalasia will donate 30mL or 60mL of venous blood, control patients will donate 30mL. No serious risks are associated with blood withdrawal. Furthermore participants will be asked to complete a questionnaire for demographic and clinical data, which isn't associated with any risks. The results of the study have no consequences for the participants. No financial compensation will be paid. The study can provide new insights in the pathogenesis of achalasia and possibly offer new targets for therapy and diagnosis, which may benefit all patients with achalasia.

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

Patients with achalasia:
- Diagnosis of achalasia confirmed by:
- Oesophageal manometry; aperistalsis, LOS dysrelaxation and hypertensive LOS (>10mmHg).
- Barium oesophagogram; delayed emptying, aperistalsis and dilatation of the oesophagus with narrowing of the distal oesophagus.
- Eckhardt score * 2.
- Age 18-75 years.
- Written informed consent;Healthy controls:
- Age 18-75 years.
- Written informed consent

Exclusion criteria

Patients with achalasia:
- Pseudoachalasia
- Chagas disease
- Upper gastrointestinal malignancy;Healthy controls:
- Symptoms suggestive of oesophageal disease.

- History of malignancy.
- History of diseases affecting the upper gastrointestinal tract (gastro-oesophageal reflux disease, eosinophilic oesophagitis)
- Pseudoachalasia
- Chagas disease
- Autoimmune diseases

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-04-2012
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO

Date:	03-04-2012
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	NL38661.018.12