Determination of neutrophils response to gluten and development of a novel less invasive assay to diagnose gluten-related diseases.

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The main objective of this study is to investigate the migratory behaviour of neutrophils isolated from healthy individuals and gluten-related disease patients* blood to develop a diagnostic tool for gluten-related diseases that can replace biopsy…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON54481

Source
ToetsingOnline

Brief title
Neutrophil migration in gluten-related diseases (Granrose).

Condition

- Gastrointestinal inflammatory conditions

Synonym
celiac disease, Gluten intolerance

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht

Source(s) of monetary or material Support: Ministerie van OC&W,Europese Unie

Intervention

Keyword: Gluten, Granulocytes, Neutrophil migration, Receptor

Outcome measures

Primary outcome

Our primary goal is to confirm the differences in neutrophil migration behaviour between control and celiac disease patients as observed in the American study, for the Dutch situation, and to add non-celiac glutensensitivity patients* neutrophils to the study in order to get insight in both gluten-related diseases that allows us to develop a diagnostic kit based on the obtained results. For this purpose we will set up the migration assay to investigate neutrophils migration to gluten in these three study groups.

Secondary outcome

We intend to find a panel of biomarkers associated with the migration capacity by performing RNA sequencing on isolated neutrophils from all three study groups. RNA sequencing is an adequate and valid method to obtain important and extensive information on the activation state of cells. This approach largely increases the possibility to find shared values and differences between the groups and allows us to get information that helps to understand underlying mechanisms that are at the basis of the observed differences in neutrophil migration behavior. Secondly, we will perform HLA-DQ2/DQ8 genotyping; since virtually all celiac disease patients carry these haplotypes (>97%) it will be important to determine these haplotypes in our participants in order to properly define the study groups. We will measure celiac markers in serum at

time of assay as an essential check for the in-remission state of the disease

in celiac disease patients and to exclude celiac disease in our healthy control

group.

Study description

Background summary

Celiac disease is an autoimmune enteropathy triggered by gluten containing cereals in genetically predisposed individuals. At immunological level, celiac disease is characterized as a Th1/Th17-mediated autoimmune disease with high mucosal titers of interferon-γ, and for this reason, throughout the years much research effort has been put into studying the adaptive immune response. In recent years, though, several studies showed involvement of the innate immunity and hence provided new insight into our understanding of how gliadin triggers inflammatory responses. Of particular interest for this application is the observation that gluten appears a potent chemoattractant factor for neutrophils. To what extent neutrophil function adds to, or protects against, gluten intolerance still needs vigorous investigation. More recently, our preliminary data revealed a distinct neutrophil migration behavior towards gliadin in patients with celiac disease versus healthy controls in the United States of America.

Study objective

The main objective of this study is to investigate the migratory behaviour of neutrophils isolated from healthy individuals and gluten-related disease patients* blood to develop a diagnostic tool for gluten-related diseases that can replace biopsy and detect a gluten-associated disease even if the patient is on a gluten-free diet. Our secondary objective is to find biomarkers associated with neutrophil immune function by the determination of expression levels of cell-specific immune mediators.

Study design

Neutrophils will be isolated from venous blood from healthy volunteers, celiac and non-celiac gluten sensitive (NCGS) patient populations. One part of the cells will be subjected to a migration assay and migration towards gluten will be monitored. Another part of the cells will be used for measuring expression levels of neutrophil immune activation and migration markers (for example: receptors that fulfill their function in neutrophil migration). The data together will complement each other and allow to get insight in neutrophil

migration and activation behavior in response to gluten.

Study burden and risks

Participating in this study does not lead to potential risks for the individual participants. The only associated risk of participating in this study is the blood draw procedure that may lead to a small transitory bruise, and dizziness at the moment of blood sampling. This is a simple study in which we only require a single-time blood sampling and completing a questionnaire; the amount of time spent in the MUMC+ for this study approximately 30 minutes. No changes in lifestyle habits will be requested.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Age: 20-60 years old

Furthermore:
- Biopsy proven celiac disease patients in remission, on a strict gluten-free diet since at least 3 months
OR
- Non-celiac gluten sensitive (NCGS) patients, reporting gastrointestinal or extra-intestinal symptoms within 8 hours after gluten consumption, in whom celiac disease has been ruled out by means of serology and/or biopsy, and on a gluten-free diet since at least 3 months
OR
- Healthy volunteers without celiac disease or NCGS, who do not state any symptoms after ingesting gluten

Exclusion criteria

- Gastrointestinal, genitourinary or immune diseases that can affect interpretation of the results
- Pregnancy
- Use of antibiotics or immunosuppressive drugs within 90 days prior to the study
- Excessive use of drugs or alcohol
- Participation in any other scientific study that may interfere with the present study

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-04-2022
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	02-03-2021
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 29405
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	Netherlands Trial Register (NTR) - nummer volgt
CCMO	NL74741.068.20
OMON	NL-OMON29405

Study results

Date completed: 31-01-2024

Summary results
Trial ended prematurely