Dendritic cell and B cell response to Campylobacter predisposing to Guillain-Barré syndrome.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peripheral neuropathies
Study type	Observational invasive

Summary

ID

NL-OMON34577

Source
ToetsingOnline

Brief title
DC/B response in GBS

Condition

- Peripheral neuropathies

Synonym
acute inflammatory demyelinating polyneuropathy, no lay-term

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Stichting Spieren voor Spieren

Intervention

Keyword: Campylobacter jejuni, Dendritic cells, Guillain-Barré syndrome, Immune response

Outcome measures

Primary outcome

The DC response to LOS as determined by: 1) B-cell proliferative capacity; 2) production of cytokines, including interferon (IFN)-β, interleukin (IL)-6, IL-10, IL-12 and tumor necrosis factor (TNF)-α; and 3) expression of differentiation markers, including CD40, CD80, CD86 and HLA-DR.

Secondary outcome

Gene expression profile of DC stimulated with C. jejuni LOS of (ex-)GBS patients and healthy controls.

Study description

Background summary

Campylobacter jejuni is the predominant preceding infection in Guillain-Barré syndrome (GBS) and is associated with severe weakness and poor prognosis. Molecular mimicry between C. jejuni lipo-oligosaccharides (LOS) and gangliosides induces cross-reactive antibody responses precipitating peripheral nerve damage. This aberrant immune response after C. jejuni infection only occurs in a minority of susceptible persons. Dendritic cells (DC) are known to orchestrate the immune response to infection. In recent pilot studies we found that DC and B-cell responses to C. jejuni LOS differ significantly between persons. High responders may be at risk to develop GBS after C. jejuni infection. We hypothesize that the DC and B-cell response to C. jejuni LOS defines the constitutional susceptibility to develop GBS after C. jejuni infection.

Study objective

The primary objective is to determine whether the DC/B-cell response to C. jejuni LOS differs in (ex-)patients with C. jejuni-related GBS compared to healthy controls. Secondly, we aim to define the variation in DC/B-cell

response to C. jejuni LOS in healthy controls. Finally, using gene expression profiles we will define the crucial DC molecules that determine a high DC/B-cell response to C. jejuni LOS.

Study design

Cross-sectional observational cohort study and longitudinal observational cohort study

Study burden and risks

Subjects will be asked to visit the Outpatient clinic neurology. Blood will be drawn to isolate white blood cells and to isolate DNA. These samples will be obtained in less than 10 minutes and carry negligible risks.
The identification of host factors that cause GBS will be of benefit to future patients, since persons could be identified with a high risk of developing GBS after C. jejuni infection. This is important for epidemiological studies in GBS and for excluding persons in vaccination studies for C. jejuni. In addition, understanding the activation of DC by C. jejuni may provide a rationale to develop new treatments that interfere with the early immune response, preventing the subsequent activation of B cells. This approach will add to current therapeutic strategies that target the effector phase of the disease, such as IVIg, plasmapheresis and complement inhibitors.

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

Healthy controls (partners, non-related family members or friends of the (ex)-GBS patients):
- Age 18 years or older
- Written informed consent given by the subject.

Ex-GBS patients:
- Fulfilling the diagnostic criteria for GBS (Asbury, 1990)
- Culture-proven and/or positive serology for C. jejuni (at time of diagnosis).
- Current age: 18 years or older
- Diagnosis of GBS was made after 1987 and at least one year before inclusion in the study.
- Patients were treated at the ward of the department of Neurology, Erasmus MC, or at the Sophia Children*s Hospital.
- Written informed consent was given by the subject.

Exclusion criteria

Both groups:
- Additional diseases or disorders at the time of diagnosis or at time of blood sampling that may influence the endpoints:
*autoimmune diseases (like multiple sclerosis, psoriasis, Crohn*s disease, ulcerative colitis, hepatitis, rheumatoid arthritis, SLE and other systemic diseases)
*acute and chronic infectious diseases (like infectious mononucleosis, HIV/AIDS)
*malignancies (not in remission);- Medicines at time of blood sampling that may affect endpoints (i.e. inflammatory processes):
*NSAIDs, corticosteroids, cyclosporine
*Cytostatic compounds
*Cytokines (analogues) and biologicals
*Intravenous immunoglobulins.

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):	01-05-2011
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	04-10-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL33335.078.10