The antibody response to pneumococcal vaccination in patients with inflammatory bowel disease patients treated with immunosuppressive agents

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Primary objective: to determine the vaccine efficacy of PCV13 plus PPV23 (2-month series) in cases, i.e. IBD patients treated with immunosuppressive agents, vs controls. Secondary objectives: - To assess if the use of a TNF-alpha inhibitor affects...

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

Summary

ID

NL-OMON45696

Source
ToetsingOnline

Brief title
PNEUMOREACT

Condition

- Gastrointestinal inflammatory conditions
- Immune disorders NEC

Synonym
antibody response, protection after vaccination

Research involving
Human

Sponsors and support

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

Intervention

Keyword: immunosuppressive agents, Inflammatory bowel disease, pneumococcal vaccination, vaccine efficacy

Outcome measures

Primary outcome

The ratio of the anti-pneumococcal antibodies measured before and four to six weeks after pneumococcal vaccination (PCV13 administered at Week 0 and PPV23 administered at Week 8). An adequate response is considered as a 2-fold increase in anti-pneumococcal antibodies.

Secondary outcome

The difference in response rates to pneumococcal vaccination between the control and intervention groups.

Study description

Background summary

Immunosuppressive agents form a major component in the treatment of inflammatory bowel disease (IBD). Immunosuppressive agents falls apart in three main categories, i.e. corticosteroids, disease-modifying anti rheumatic drugs (DMARDs) (1). The mechanism of action of corticosteroids is blockage of the early manifestations of inflammation such as vasodilation, vascular permeability and infiltration of neutrophils. DMARDs suppress the immune system by inhibiting proliferation and activation of lymphocytes. TNF-alpha inhibitors are the principle biologicals in the treatment of IBD; it has been demonstrated that TNF-alpha plays a crucial role in the pathophysiology of IBD (1, 2). However, immunosuppressive agents increase the risk of infection, notably TNF-alpha inhibitors strongly suppress the immune system (3-6). Therefore, according to European and American guidelines, pneumococcal vaccination is

indicated for IBD patients treated with immunosuppressive drugs to prevent pneumococcal infection (4, 5).
The suppressed state of the immune system impairs the antibody response to vaccination, though there are only few data available on the efficacy of pneumococcal vaccines in immunocompromised populations. Some investigators studied the antibody response in inflammatory bowel disease (IBD) patients on immunosuppressive agents after vaccination with the 23-valent pneumococcal polysaccharide vaccine (PPV23) (3, 7, 8); and found lower response rates (57.6%) among patients treated with anti-TNF compared to IBD patients only treated with mesalazine (response rates 88.6%) (7). However, to the best of our knowledge, vaccine efficacies of PCV-13 plus PPV-23both (in series whereby the PPV-23 is administered two months after the PCV-13) in immunosuppressed patients with IBD has not been evaluated systematically to date. Furthermore, the ideal time interval between vaccination and treatment initiation with anti-TNF to reach the best antibody response remains to be elucidated.
We hypothesize the following:
Hypothesis 1: IBD patients treated with immunosuppressive agents have a diminished anti-pneumococcal antibody response to pneumococcal vaccination.
Hypothesis 2: Use of a TNF-alpha inhibitor is associated with a lower antibody response after pneumococcal vaccination than use of (DMARDs) and/or corticosteroids. Use of either high dose monotherapy with a TNF-alpha inhibitor, or use of standard dose TNF-alpha inhibitor plus additional immunosuppressive drugs, is associated with an even lower antibody response after pneumococcal vaccination.
Hypothesis 3: A longer time-interval between pneumococcal vaccination and treatment initiation with TNF-alpha inhibitors is associated with a better antibody response.

Study objective

Primary objective: to determine the vaccine efficacy of PCV13 plus PPV23 (2-month series) in cases, i.e. IBD patients treated with immunosuppressive agents, vs controls.
Secondary objectives:
- To assess if the use of a TNF-alpha inhibitor affects the anti-pneumococcal antibody response in a different way than DMARDs and/or corticosteroids do and if either increased dose monotherapy with a TNF-alpha inhibitor further affects the immune response.
- To determine the ideal time-interval between pneumococcal vaccination and treatment initiation with TNF-alpha inhibitors to reach an adequate antibody response.

Study design

Prospective cohort study.

Study burden and risks

Participants do not benefit directly from participation in this study except for that appropriate vaccination according to guidelines is warranted and safeguarded. However, the control group will be better informed on the result of their pneumococcal vaccination because according to routine procedures, the anti-pneumococcal titre would not have been assessed. The additional risk of participation is limited to the drawing of two blood samples (10mL each) at two different time points and only applies to the control group, as for IBD patients the titre assessment belongs to the standard procedure.

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

- Age > 18 years old
- On treatment with an immunosuppressive agent or planned treatment start with a TNF-alpha inhibitor within 3 months after recruitment
- Indication for pneumococcal vaccination (PCV13 plus PPV23)
- Able to give informed consent
- Control group: diagnosed with IBD, not treated with immunosuppressives.

Exclusion criteria

- Diagnosis of an immune deficiency disorder
- Age < 18 years
- Control group: treatment with immunosuppressive drugs

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-12-2016
Enrollment:	178
Type:	Actual

Ethics review

Approved WMO Date:	24-11-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2017
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

ID: 29135
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL58768.018.16
OMON	NL-OMON29135