Chronic rhinosinusitis and nasal polyposis a GA2LEN cohort study

Published: 18-04-2007
Last updated: 08-05-2024

1. To integrate ENT specialists into the GA²LEN project in co-operations with internal medicine, allergists and pneumologists.2. To characterize patients with upper airway diseases on the basis of clinical parameters, infectious agents, inflammatory...

Ethical review	Approved WMO
Status	Pending
Health condition type	Upper respiratory tract disorders (excl infections)
Study type	Observational invasive

Summary

ID

NL-OMON31056

Source
ToetsingOnline

Brief title
Chronic rhinosinusitis and nasal polyposis a GA2LEN cohort study

Condition

- Upper respiratory tract disorders (excl infections)

Synonym
nasal polyps, sinusitis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: europese unie;GA2LEN

Intervention

Keyword: chronic rhinosinusitis, european cohort study, nasal polyps

Outcome measures

Primary outcome

Characterization and further differentiation of chronic sinus disease based on clinical and biological parameters.

The following inflammation parameters will be particularly analyzed:

A) Immunohistochemical staining for eosinophils (H&E), neutrophils (H&E, MPO), macrophages, T-cells, B-cells (frozen sections)

B) On tissue homogenates:

* Pro-inflammatory cytokines: IL-1*, TNF-*

* Eosinophilic inflammation: ECP, eotaxin, IgE

* Neutrophilic inflammation: IL-8, MPO

* T cell markers: sIL-2R*, IFN-*(Th1), IL-5(Th2)

* TGF-beta 1

C) On nasal secretions:

* ECP

* TGF-beta

* IgE

* Il-1beta

* TNFalpha

* Il8

* Il5? NP

* MPO

D) Full blood and eosinophil count

Secondary outcome

(1) Determine T-cells scources for Th1 cytokines (INF-g), Th2 cytokines (IL-4

and IL-5, and T regulatory asscoiated expression of CD25, foxP3, IL-10, and

TGF-b.

(2) Determine activation status of blood born T regulatory cells

Study description

Background summary

TITEL : Chronic rhinosinusitis and nasal polyposis a GA2LEN cohort study

Chronic rhinosinusitis is one of the most common health care problems, with significant direct medical costs and severe impact on lower airway disease and general health outcomes.
Rhinosinusitis remains a significant health problem with a considerable socio-economic burden and is still increasing in prevalence and incidence. US data of 1997 indicate a prevalence of app. 15% of chronic rhinosinusitis patients (defined as having *sinus trouble* for more than 3 months in the year before the interview) in the general population.(1) In the period from 1985 to 1992, the number of antibiotic prescriptions for sinusitis rose from 7.2 million to 13 million per year.(2) According to figures from IMS Health, an internationally accepted information provider for the pharmaceutical and health care industries, acute sinusitis was diagnosed 6.3 million times and chronic sinusitis 2.6 million times in Germany, a European country with 81 million inhabitants, over the course of one year (7/2000-6/2001), resulting in 8.5 million and 3.4 million prescriptions, respectively. The number of diagnoses of

nasal polyposis was approximately 221,000. (3)
In order to summarize the current knowledge of pathophysiology, as well as guidelines for the therapeutic and diagnostic management of sinus disease, position papers have recently been developed in the US (4) and Europe (5), which also identify deficits in our understanding. (4)
Rhinosinusitis is a heterogeneous group of diseases, with different underlying etiologies and pathomechanisms, and may represent an umbrella, covering different disease entities. Rhinosinusitis is diagnosed based on symptoms and duration of symptoms, clinical examination, nasal endoscopy and CT-scan. However, the pattern of symptoms and signs is overlapping in all patients with chronic sinus inflammation, whether they have formation of nasal polyps (NP) or not (CRS It is currently not understood whether acute recurrent rhinosinusitis necessarily develops into chronic rhinosinusitis, which then possibly gives rise to polyp growth, or whether these disease entities develop independently from each other. All of these items may be referred to *rhinosinusitis*, meaning the *inflammation of the nose and the sinuses*; however, for clinical and research purposes, a differentiation of these identities should be preferred. For this purpose, we differentiate between acute rhinosinusitis (ARS), chronic rhinosinusitis (CRS) without polyps and chronic rhinosinusitis with nasal polyps (NP), and omit an ill-defined group of *hyperplastic chronic rhinosinusitis*, which might be included in CRS, or represent an overlap between CRS and NP.). As a result, all chronic sinus disease is considered as one disease spectrum, *chronic rhinosinusitis*.
So far, nasal polyp formation in specific conditions such as cystic fibrosis (CF) and allergic fungal sinusitis (AFS) can be differentiated as disease entities, based on genetic defects in CF and a specific IgE-mediated immune response to fungi in AFS respectively. For the majority of chronic sinusitis cases, however, classification awaits further insights into pathomechanisms and the introduction of appropriate disease markers. Such markers could possibly be derived from 1) inflammatory cells, such as eosinophils and neutrophils, which can be found in increased numbers in some forms of sinus disease, 2) from the Th1/Th2 paradigm, possibly also involving T regulatory cells, and the cytokines released from those cells, 3) from remodelling processes linked to fibrosis or oedema formation, or 4) from innate or adaptive immunity products such as toll-like receptors or immunoglobulins. Differences in some of these markers in sinus disease versus nasal control tissue have been described (6), but these have not proven useful to differentiate disease entities of CRS. For example, interleukin (IL)-5, an eosinophil survival and differentiation factor, and eosinophil-cationic protein (ECP), an indicator for eosinophil activation, have been found to be significantly increased in NP versus controls. (7) Only recently, differences in the expression of metalloproteinases and their inhibitors could be demonstrated in CRS versus NP mucosal tissue. (8)
By characterizing the patients on the basis of clinical parameters, infectious agents, inflammatory mechanisms(chemokines, cytokines), and remodeling processes(growth factors), the term CRS will probably be further differentiated into smaller disease entities, which might be treated differentially.

Study objective

1. To integrate ENT specialists into the GA²LEN project in co-operations with internal medicine, allergists and pneumologists.

2. To characterize patients with upper airway diseases on the basis of clinical parameters, infectious agents, inflammatory mechanisms and remodeling processes.

3. To differentiate the term chronic rhinosinusitis further to smaller disease entities based on clinical and biological parameters.

Study design

This cohort study is subdivided into two parts which will be performed independently from each other. The first part encompasses a cross-sectional study which will aim to differentiate chronic sinus disease.

Study burden and risks

The major burden of the study is the extra time for the patient, whcih is one hour during visits that the patient is already in the hospital for regular visits. None of the procedures here have major safety concerns.
Skin testing: Severe reactions are rarely if ever seen using this technique. Centres will however be instructed to keep adrenaline available. Itching is a common problem but disappears after 30 minutes.
Venesection: This may cause a little discomfort and can cause minor bruising. All phlebotomists will be trained in aspects of safety relating both to themselves and the patients.
collecting nasal secretion: minimally uncomfortable

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

1. The subject understands the study procedures and agrees to participate by signing the consent form.
2. The subject is male or female, at least 18 years of age but no more than 60 years of age
3. Subjects must be in good health, free of any clinically significant disease that would interfere with the study or procedures or compromise his/her safety.
4.Diagnosis of chronic rhinosinusitis:
The diagnosis of chronic rhinosinusitis (with or without nasal polyps, including fungal disease, Cystic fibrosis, etc.) based on the EP3OS definition ;For controls: Controls are patients undergoing surgery such as septoplasty or septorhinoplasty, who have no medical history or symptoms of any form of chronic rhinosinusitis

Exclusion criteria

1. Patients with a recent acute exacerbation of rhinosinusitis (past two weeks) are not allowed to participate
2. The subject had functional endoscopic sinus surgery (FESS) before, with removal of parts of the lateral nasal wall. Polypectomy, septal or inferior turbinate surgery is allowed.
3. Women must not be pregnant or breast feeding
4. The subject is a current or recent past abuser of alcohol or illicit drugs
5. The subject has a history of malignancy, is known to be positive for HIV, has immunodeficiencies or other states that are considered to interfere with study conduct or scientific interpretations.
6. Subjects must not be known to have sarcoidosis
7. Subjects must not be known to have any type of vasculitis (including Wegener)
8. Subjects must not be known to be positive to hepatitis B surface antigen or C antibodies.
9. The subject cannot read or comprehend written material, or is in the opinion of the investigator, for other reasons unlikely to understand and follow the study procedures.

10. The subject is mentally or legally incapacitated preventing informed consent from being obtained.
11. Medication: For Visit 2 a wash-out period for the medications (oral steroids 4 weeks, Nasal steroids 2 weeks, anti-leukotrienes 2 weeks) is mandatory, for visit 1 the wash-out period is advisable although patients using this medication can be included.
12. Inhalation steroids for asthma are permitted but should be documented in the questionnaires.

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:	Pending
Start date (anticipated):	01-02-2007
Enrollment:	125
Type:	Anticipated

Ethics review

Approved WMO

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	NL16401.018.07