Study of n-Acetyltransferase-1 en -2 (NAT-1, NAT-2) and other polymorphisms in persons with contactallergy for p-Phenylenediamine (PPD)

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Determine the number of variants of NAT-1 and NAT-2 in patients with contact-allergy to PPD.Exploring polymorfisms in genes that are involved in the production and regulation of cytokines that modulate immunological defence reactions.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Epidermal and dermal conditions
Study type	Observational invasive

Summary

ID

NL-OMON30831

Source
ToetsingOnline

Brief title
PPD-allergy and polymorphisms

Condition

- Epidermal and dermal conditions

Synonym
contact allergy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

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

Intervention

Keyword: contactallergy, NAT, polymorphism, PPD

Outcome measures

Primary outcome

The odds-ratios of the proportional frequencies of NAT-1 and NAT-2 variants in

patients with a contactallergy to PPD.

Secondary outcome

n.a.

Study description

Background summary

There are indications that the growing use of hair-dye and henna-tattoos is associated with an increase of the number of people with a contact-allergy to the substance of p-Phenylenediamine (PPD), a component of hair-dye. Every individual possesses the enzymes n-Acetyltransferase-1 (NAT-1) and n-Acetyltransferase-2 (NAT-2). NAT-1 and -2 are involved in transforming PPD. In the general population however, there are different genetically determined differences in the structure of NAT-1 and NAT-2. In some individuals NAT-1 and NAT-2 operate fast (fast acetylators) and in others slowly (slow acetylators), mixed-variants also exist.
Patients with eczematous skin reactions and a suspicion of contact-allergy are routinely being tested in the department of Dermatology by means of a patch test. In the standard patch test people are tested on a series of frequent allergens (the European Standard series). This standard series also contains the allergen PPD. Today about 2 to 3 % of all tested patients in Europe have a contact-allergy to PPD. Skin reactions in PPD-allergy can be severe.
There are signs that the acetylatorstatus (the slow variant in particular) is associated with a higher risk of developing a PPD-contact-allergy. Previous studies however have been performed in relatively small series, in which the clinical relevance of the reaction on PPD hasn*t been well characterized. To be able to respond more adequately to the question of the role of acetylatorstatus in PPD-allergy, it is desirable to know how the distribution is between *slow* versus *fast* and mixed-variants in a well-documented case-series of

dermatological patients with PPD-allergy.
In studies of other T-cell mediated reactions indications have been found that polymorfisms in genes that code for certain cytokines (e.g. TNF-α, MnSOD and Inteleukine 1-β) are involved in the severity of the immunological defence reactions on exogenous substances.

Study objective

Determine the number of variants of NAT-1 and NAT-2 in patients with contact-allergy to PPD.
Exploring polymorfisms in genes that are involved in the production and regulation of cytokines that modulate immunological defence reactions.

Study design

In this study a small amount (10 ml) of blood is needed from patients with PPD-allergy. Each patient that has a positive reaction on PPD or the chemically closely related p-Toluenediamine (PTD) in the routinely taken patch-test at the department of Dermatology in the University Medical Centre Groningen (UMCG) are asked if they are prepared to give a blood sample for this study. When permission is given, blood will be taken in the laboratory of the UMCG and will then be frozen for storage and processing.
The stored blood samples are made anonymous and only with a code it can be traced back to the specific patientfile. The key of the code is in the possession of the main investigator prof. P.J. Coenraads.
To achieve a large enough case-series, considered the amount of patients that have a positive reactions to PPD, the collection of blood samples will take a minimum of 4 years. According to the power-calculation 400 blood samples from PPD-allergic patients will be needed. To realise this number, cooperation has been obtained from the Dermatology departments of the University Medical centre St. Radboud in Nijmegen and the Vrije Universiteit Medical Centre in Amsterdam. Processing and analysis of the anonymous blood samples will take place in cooperation with the department of Toxicology/Ecotoxicology from the University of Trier (Germany) as described in the manuscript from Blömeke et al.

Study burden and risks

All patients that are considered for participating in this study because of the results of the allergy-test will be informed verbally. Subsequently the patient will receive written information signed by the investigator and an independent physician, in which the objective and design is further explained. Verbally as well as in writing the patient will be explicitly told that he can quit participating in the study, without this having any negative influence on the treatment of the patient in the UMCG. When a patient decides to participate in the study, written informed consent will be asked by signing the informed consent form both by the patient and the investigator. The effort of patients

will be kept to a minimum. Blood will be taken by experienced and qualified employees from the laboratory of the UMCG. The investment in time will be about 5 to 10 minutes per patient and will only include giving a blood sample. It will not be necessary to fill in questionnaires or any other forms.

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

positive patch-test on p-phenylenediamine or p-toluenediamine

Exclusion criteria

legally incompetent

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-09-2007
Enrollment:	400
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	11-09-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Not approved

Date:	17-12-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	08-04-2020
Application type:	Amendment

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

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	NL19111.042.07