Study of individual N-acetyltransferase 1 activity in persons with contact allergy for para-phenylene diamine (PPD).

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

Summary

ID

NL-OMON34651

Source
ToetsingOnline

Brief title
PPD-allergy and N-acetyltransferase 1 activity.

Condition

- Epidermal and dermal conditions

Synonym
allergic contact dermatitis, contact allergie

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: contact allergy, NAT-1 activity, PPD

Outcome measures

Primary outcome

- N-acetyltransferase 1 (NAT-1) activity within subjects allergic to PPD,

compared to subjects without a PPD allergy. The NAT-1 activity will be measured

in whole blood, in the whole PBMC population and in the CD3+, CD4+ and CD8+

T-cells seperately.

Secondary outcome

- Quantification of cytokines in plasma.

- Genotyping for the NAT-1 gene and determining the odds ratio of proportional

frequencies of NAT-1 variants.

- Determining the NAT-1 protein leven in leucocytes/T-cells.

- Determining the promotor region methylation status.

Study description

Background summary

In a recent study (on NAT polymorphisms and PPD) there was found a significant difference in acetylation activity (through NAT-1, a phase II enzyme which provides detoxification) between PPD allergic subjects and healthy volunteers. In the allergic group, half of the acetylation products were found, compared to the healthy subjects. However, no difference was found between the NAT-1 genotype between both groups, i.e. both PPD allergic patients and healthy subjects were indentified as being normal acetylators and not being slow acetylators. For the time being, the difference in acetylation activity between the two groups can't be explained by the known genetic facor. There appears to be unknown genetic, epigenetic and/or environmental factors playing a role in the deviating N-acetylation. That's why we request for expanding the study "Study of n-Acetyltransferase-1 en -2 (NAT-1, NAT-2) and other polymorphisms in

persons with contactallergy for p-Phenylenediamine (PPD)", NL19111.042.07.

Study objective

The aim of this study is to detect the hitherto unknown factors which possibly can explain the difference in acetylation. Therefore we need to collect blood from PPD allergic patients and healthy volunteers, to determine not only the genotype, but also N-acetylation activity of whole blood and peripheral blood mononuclear cells (PBMCs). Besides determining N-acetylation activity of PBMCs as a whole group, different subpopulations of T-cells will be analyzed too, to determine their specific role. Other, possible explanations for the differences in acetylation activitynare differences in NAT-1 protein level in leucocytes and T-cells and the methylation status of NAT-1's promotorregion. The blood will be analyzed for these variables too.

Study design

In this study an amount of 300ml blood is needed from patients allergic to PPD. Each patient that has a positive reaction on PPD 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. Also patients patchtested positive for PPD in the past year, will be approached in writing. Both groups don't have to answer a questionnaire, their information is known already through their regular visits to the Dermatology department. De control group will consist of healthy volunteers who dyed their hair in the past, but didn't develop an allergic reaction anamnestically. They will partly be recruted from known PPD negative patchtested patients, with a positive history of hair, which visited the Dermatological department in the past year. They don't have to be patchtested again. When there is insufficient response, there will be an advertisement on bulletin boards in the UMCG in order to obtain healthy volunteers.(First of all via bulletin boards of the dermatology department, if needed via general bulletin boards in the UMCG, or via an advertisement in local newspapers). These volunteers will be patchtested with PPD where appropriate, to exclude a PPD allergy. For these volunteers, there has to be a period of at least 3 weeks in between the patch test and the blood drawing, to obtain reliable results. The control group has to answer a short questionnaire. Verbally as well as in writing the patients and controls 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. They have one week to think about participation. 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. When permission is given, 300ml of blood will be drawn by an experienced doctor. This will be processed within 24 hours and then will be stored frozen (-80 C or in nitrogen) until further analysis will be executed. The stored blood samples are stored anonymous. 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 3 years. According to the power-calculation 30 blood samples from PPD-allergic patients and from 30 healthy subjects will be needed. 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).

Study burden and risks

All patients that are considered for participating in this study because of the results of the allergy-test will initially be informed verbally (when patchtested routinely) or in writing (when they had a positive patchtest on PPD in the past year). 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 explicitely 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 and will comprise in all cases of a single blood donation of 300ml, obtained through a venous puntcion by an experienced doctor. In case of healthy subjects with no allergic reaction towards hairdyeing anamnestically, a PPD patchtest will be applied to exclude a PPD allergy. A PPD patchtest doesn't comprise a big risk; in fact it is regarded as safe and not causing active sensitization (Contact Dermatitis 2007; 57(2):133-4). Where appropriate, a short questionnaire has to be completed. The investment in time in total will comprise a maximum of 15 minutes per patient and will at least include donating blood and in some cases completing a short questionnaire and/or a PPD patchtest. The PPD patchtest comprises the application of the patch in the hopital (2.5 minutes), whereupon subjects can return to their homes. After 48 hours the patch can be removed by the patient himself, after 72 hours the patchtest reading will be performed in the UMCG by a doctor (2.5 minutes). At least 3 weeks after the PPD patch test, the blood drawing may take place. In total, these subjects are coming to the UMCG three times.

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

patients: positive patch test on para-phenylene diamine (PPD)
controls: negative patch test on para-phenylene diamine (PPD) and exposure to hairdye in the past

Exclusion criteria

legally incompetent

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):	02-08-2010
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	10-06-2010
Application type:	First submission
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	NL30905.042.10