Dose range finding pilot study for diagnostic patch testing with ME-PPD

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Primary Objective: Pilot study to identify the optimal patch test concentration for detecting contact allergy to ME-PPD in subjects with a proven contact allergy to PPD, who may be allergic to ME-PPD. Hypothesis: In this study subjects will be...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Administration site reactions
Study type	Observational invasive

Summary

ID

NL-OMON43828

Source
ToetsingOnline

Brief title
ME-PPD: 0.1%, 0.25%, 0,5%, 1% and 2%.

Condition

- Administration site reactions
- Allergic conditions
- Epidermal and dermal conditions

Synonym
allergic contact dermatitis, contact eczema

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Proctor&Gamble

Intervention

Keyword: 2-Methoxymethyl-p-phenylenediamine (ME-PPD), Allergic contact dermatitis, Epicutaneous patch-testing, Para-phenylenediamine (PPD)

Outcome measures

Primary outcome

The primary study parameters are the results of the epicutaneous patch tests

for the different concentrations of ME-PPD and the results of the open use

test, graded according to guidelines of the International Contact Dermatitis

Research Group (ICDRG): - , +?, + , ++ , +++ or IR (irritation response).

Secondary outcome

The secondary study parameters are the results of the epicutaneous patch tests

to the MAPPD and DAPPD graded according to the ICDRG : - , +?, + , ++, +++ or

IR (irration response).

Study description

Background summary

para-Phenylenediamine (PPD) is an organic molecule, which is used in dark hair dyes, manufactory dyes, dyed leather and rubber.(1) It is categorized in the so-called para-group of aromatic amines. PPD is used together with a coupler (e.g. m-aminophenol and resorcinol) and an oxidizing agent (e.g. hydrogen peroxide) in permanent hair dyes.(2) It is estimated that 70% of all the permanent oxidative hair dyes contain PPD.(3)

PPD is an effective hair dye because of its typical characteristics: a low molecular weight, the ability to penetrate the hair shaft and follicle, strong protein binding capacity, and rapid polymerization in the presence of a coupler and an oxidizing agent. Unfortunately these characteristics make PPD also a very potent allergen and the global cause of 4-7% of all cases of allergic contact dermatitis.(3) Symptoms may include redness (erythema), swelling (edema, papulation), itching, blistering (vesicles and bullae) and/or scaling. Although the severity of the reaction, there are still patients who keep dyeing

their hair.

Sensitization to PPD and other molecules from the para-group can also be caused by a cross-reaction between these molecules.(4,5) For example, a previously PPD- sensitized individual can develop an allergic contact dermatitis to p-Toluenediamine (PTD) without ever been in contact with that molecule. PTD is another important primary intermediate in oxidative hair dyes. The immunological causes for cross-reactivity are not fully explained yet.
Recently, a new hair dye molecule, 2-methoxymethyl-p-phenylenediamine (ME-PPD) has been developed. The introduction of a methoxymethyl side chain into PPD yielded a hair dye precursor with excellent hair colouring performance. Besides that ME-PPD has significantly reduced skin sensitizing properties compared to PPD and PTD.(6)

In a previous study cross-elicitation reactions to ME-PPD were investigated in PPD-allergic individuals with a documented history of hair dye related allergy and a positive diagnostic patch test response to PPD. ME-PPD was investigated under use conditions by testing 2% ME-PPD in a hair dye test product for 30 minutes on the volar side of the forearms, followed by rinsing.
Cross-reactivity to the ME-PPD containing hair dye test product was elicited in 9/30 (30%) of PPD allergic individuals. (7) A total of 21 patients showed a positive reaction to 2% PPD containing hair dye test product investigated under the same use conditions as for ME-PPD. Six out of these 21 (29%) subjects showed a positive reaction to the ME-PPD hair dye product.

In the current study we will investigate sensitization to ME-PPD by diagnostic patch testing with different concentrations ME-PPD, to identify the optimal patch test concentration. Moreover an open patch test will be performed on the volar side of the forearms with ME-PPD 2%, PPD 2% and a control vehicle without colors to provide us insight information in the clinical relevance of a potential positive reaction to the patch test.
Furthermore we will investigate whether the assumed acetylation products of ME-PPD (monoacetyl- and diacetyl-PPD) can elicit an allergic reaction. Since we do not know why only a part of the PPD-allergic individuals gets sensitized to ME-PPD a possible explanation could be that these acetylation products could be the responsible sensitizers.

(1) Fernandez-Vozmediano JM, Padilla-Moreno M, Armario-Hita JC, Carranza-Romero C. Pattern of contact sensitization to paraphenylenediamine and its detection in hair dyes. Actas Dermosifiliogr 2011 Apr;102(3):206-211.
(2) Schnuch A, Lessmann H, Frosch PJ, Uter W. para-Phenylediamine: the profile of an important allergen. Results of the IVDK. Br J Dermatol 2008 Aug;159(2):379-386.
(3) Thyssen JP, White JM, European Society of Contact Dermatitis. Epidemiological data on consumer allergy to p-phenylenediamine. Contact Dermatitis 2008 Dec;59(6):327-343.

(4) Xie Z, Hayakawa R, Sugiura M, Koijma H, Konishi H. Ichihara G, et al. Experimental study on skin sensitization potencies and cross-reactivities of hair-dye-related chemicals in guinea pigs. Contact Dermatitis 2000 May;42(5):270-275.
(5) Mathelier-Fusade P, Leynadier F. Crossreactions in contact dermatitis. Clin Rev Allergy Immunol 1997 Winter;15(4):477-484.
(6): Goebel C, Troutman J, Hennen J, Rothe H, Schlatter H, Gerberick GF, et al. Introduction of a methoxymethyl side chain into p-phenylediamine attenuates its sensitizing potency and reduces the risk of allergy induction. Toxicol Appl Pharmacol 2014 Feb 1;274(3):480-487.
(7) Blomeke B, Pot LM, Coenraads PJ, Hennen J, Kock M, Goebel C. Cross-elicitation responses to 2-methoxymethyl-p-phenylediamine under hair dye use conditions in p-phenylenediamine-allergic individuals. Br J Dermatol 2014 Sep 18.

Study objective

Primary Objective: Pilot study to identify the optimal patch test concentration for detecting contact allergy to ME-PPD in subjects with a proven contact allergy to PPD, who may be allergic to ME-PPD.

Hypothesis:
In this study subjects will be tested to ME-PPD 0.5%, 1% and 2%, in white petrolatum . We hypothesize that the optimal patch test concentration for detecting contact allergy to ME-PPD will be 1%, comparable to the patch test concentration of PPD.

Secondary Objective(s):
1. Investigate the clinical relevance of a positive diagnostic patch test reaction to ME-PPD in subjects with a proven contact allergy to PPD, in comparison to the (possible) allergic reactions as a result of an open use test with ME-PPD 2%, PPD 2% and a control vehicle, respectively, with a use-relevant exposure duration of 45 minutes.

2.As an independent control for cross-reactivity, we will investigate whether subjects with a positive diagnostic patch test for ME-PPD, will show positive patch test reactions to the acetylation products of PPD; MAPPD and DAPPD 1%, in white petrolatum.

Study design

This is an observational pilot study with the use of epicutaneous patch-testing and an open use test. Without the use of medicinal product non-blinded and non-randomized in 44 PPD-positive subjects.

The duration for an individual participant is one week during which there will

be four visits of variable time durations.
Visit 1, day 0:
A short interview will be held to reconfirm basic information about the subject and to check the inclusion and exclusion criteria. This visit also includes the preparation of material, the application of the open use test on the volar side of the forearms and the application of the patch test on the back. This visit will take about 75 minutes. The actual patch test needs to be in situ for 48 hours.

Visit 2, day 2, 48 hours after application:
The visit will take about 15 minutes and includes removal of patch test, reading of skin reactions according to guidelines of the International Contact Dermatitis Research Group (ICDRG): - , +?, + , ++ , +++ or IR (irritation response) and photographing.

Visit 3, day 3, 72 hours after application:
The visit will take about 15 minutes and includes reading and photographing of the (possible) skin reactions at the sites of application.

Visit 4, day 7, 168 hours after application:
This visit includes the final reading and photographing of the (possible) skin reaction at the sites of applications and will take about 15 minutes.

Study burden and risks

For the epicutaneous patch test and the open use test, four visits, divided over 4 days will be planned. The first visit will take approximately 75 minutes and the remaining visits will take 15 minutes each. There will be a travelburden, but the particpants are offered the oppurtunity to perform the reading at a place of their preference (at their home or at work for example). During this study, subjects are asked to not wash or rub the test site or apply (perfumed) lotion to the test areas.

Subjects are at risk for developing an allergic skin reaction on the test sites, which can exist of redness, itch, vesicles and papules. This skin reaction is self-limiting in nature, but can be treated with a local corticosteroid cream if the reaction is inconvenient.

Participants will receive gift cards with a value of ¤100,- and reimbursement of travel expenses.

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

- A history of (mild, moderate of severe) allergic contact dermatitis after exposure to a PPD-containing product (mostly hair dye);
- A positive patch-test to PPD (1% in white petrolatum);
- Adulthood (>=18 years);
- Legal competence.

Exclusion criteria

- Skin anomalies at the volar side of the forearms or back;
- Active skin disease at the volar side of the forearms or back;
- Immunosuppressive medication (e.g. oral cortosteroïds, methotrexate, cyclosporine) during or in the previous 4 weeks of the study;
- Pregnancy or pregnancywish;
- Breastfeeding.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-11-2015
Enrollment:	44
Type:	Actual

Ethics review

Approved WMO Date:	29-10-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-05-2016
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	NL52693.042.15