A study to investigate the effect of inhaled and intranasal pathogens on pro-infammatory markers using (existing) techniques in order to acquire experience with these techniques.

Gepubliceerd: 23-08-2012 Laatst bijgewerkt: 15-05-2024

To acquire experience with sputum induction and LPS challenge techniques.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26578

Bron
Nationaal Trial Register

Verkorte titel
125633-CS0186

Aandoening

Asthma, COPD
Astma, COPD

Ondersteuning

Primaire sponsor: QPS Netherlands B.V.
QPS Netherlands BV
Petrus Campersingel 123
9713 AG
Groningen
Overige ondersteuning: QPS Netherlands B.V.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. Cellular fraction endpoints, for evaluation of total and differential cell count (analyzable sputum);
2. Sputum inflammatory cell response (i.e., number of neutrophils; responders versus non-responders; response defined as an absolute rise in sputum neutrophil counts of at least 10% from pre-challenge evaluation;
3. Soluble fraction (supernatant) endpoints, to be frozen pending analysis. Used analyses technique examples are: ELISA, RIA, Luminax for the detection of soluble inflammatory biomarkers including cytokines and mediators Including, but not limited to e.g. interleukin (IL)-8, TNF-alpha, leakage markers (e.g., alpha2-macroglobulin).

Toelichting onderzoek

Achtergrond van het onderzoek

This is a phase 0 study to investigate the effects of inhaled and intranasal lipopolysaccharide (LPS) on pro-inflammatory markers sampled by hypertonic saline-induced sputum (SI) and nasal lavage (NAL) in healthy subjects. The main objectives are to set up the SI and LPS challenge techniques, to evaluate the sampling success, to investigate the pro-inflammatory effects of inhaled and intranasal LPS, and to evaluate the repeatability of the LPS inflammatory response. In part 1 of the study LPS will be substituted by normal saline.

This study contributes to further development of medicine of obstructive airway diseases.

Subjects will be recruited in the Netherlands.

Doel van het onderzoek

To acquire experience with sputum induction and LPS challenge techniques.

Onderzoeksopzet

After spututum induction challenges, after LPS challenges and during the course of the study

(safety endpoints).

Onderzoeksproduct en/of interventie

Primary objectives Part 1:

1. To set up the SI and LPS (in part 1 substituted by Normal Saline) challenge techniques;

2. To evaluate the sampling success (i.e., the percentage of analysable sputum and NAL samples), pre- and post-LPS challenge; in terms of non-squamous cell counts (total cell numbers and differentials);

3. To identify “LPS-responders”, defined as those subjects with an absolute increase (pre- vs. post challenge) in sputum neutrophil count of >=10%.

Primary objectives part 2:

1. To investigate the pro-inflammatory effects of inhaled LPS (at a previously applied dose of 60 µg) within the lower airways of healthy subjects, by hypertonic saline-induced (NaCl 4.5%) sputum;

2. To investigate the pro-inflammatory effects of low-dose intranasal LPS (at a previously applied dose using the split nose method) within the upper airways of healthy subjects, using NAL;

3. To evaluate the repeatability of the LPS inflammatory response, all procedures need to be repeated with the same subjects in a second identical study period;

4. Additional subjects need to be tested, to validate the techniques used.

Intervention Part 1:

On day 1, after baseline spirometry, sputum will be induced by inhalation of hypertonic saline (NaCl 4.5% aerosol generated by ultrasonic nebulization), during 3 times 5 min (at approximately 15 min intervals). Sputum samples will be collected in a clean plastic container on melting ice and processed within 2 hrs. This will serve as the baseline sputum sample. On day 2, an inhaled LPS* challenge will be performed (approx. 24 hrs after baseline SI) followed by SI 6 hrs later (approx. 30 hrs after baseline SI); to assess the acute LPS effects in the lower airways. On day 3, an intranasal LPS challenge will be performed, using the split-nose method, followed by a NAL 6 hrs post challenge.

Intervention Part 2:

Part One study participants (those actually exposed to SI and LPS challenge, will also be invited to participate in a second study period (washout >=3 weeks), identical to the first study period (to test SI and LPS challenge repeatability). Only those will be invited again, from whom an analysable sputum sample could be obtained during Part One. To validate the techniques used, additional subjects will be included, each of them will participate in two identical study periods as well. For individual subjects, all study related measurements will be performed in similar within-day time frames (±3 hrs).

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Healthy Male/Female subjects, aged 18-55 yrs (inclusive);

2. FVC, FEV1 80% ; FEV1/FVC ratio 0.75;

3. Oxygen saturation 94% (pulsoximetry);

4. Normal blood pressure (SBP 90-150, DBP 60-90 mmHg, inclusive) and pulse (45-100 bpm, inclusive);

5. ECG without clinically relevant abnormalities;

6. Normal body temperature (<37.5 °C);

7. Normal blood leukocyte count;

8. Normal CRP;

9. Adequate contraception (from screening to follow-up);

10. Must be able to return <10 days after LPS challenge, for follow up.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. History of upper and lower airway infection <4 wks;

2. Relevant atopy;

3. Current smokers (ex-smoker >1 yr, <10 packyrs, inclusive);

4. Positive metacholine inhalation test with a post challenge FEV1 decrease <20% (PC20), <16 mg/ml;

5. Any relevant upper airway condition (e.g. serious septal deviation, status post any upper airway surgery, chronic sinusitis or polyposis, at the discretion of the investigator);

6. History of clinically relevant pulmonary or cardiovascular disease;

7. Any inhaler or intranasal medications – other medications, at the dis-cretion of the investigator;

8. Positive pregnancy test or lactation;

9. Unable to perform any of the study-related tests.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	27-08-2012
Aantal proefpersonen:	10
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	23-08-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 36988
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3439

Register	ID
NTR-old	NTR3590
CCMO	NL41617.056.12
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON36988

Resultaten

Samenvatting resultaten
N/A