A randomized, double-blind, placebo-controlled study of ascending single low doses of LPS administered intravenously to healthy volunteers to assess the dose-response relation.

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To assess the relationship between administration of low doses of LPS (0.5, 1 and 2 ng/kg bodyweight) and the inflammatory response (cytokine levels and hs-CRP) in healthy male volunteers;To assess the duration of tolerance/paralysis of the immune...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON37142

Source
ToetsingOnline

Brief title
LPS challenge in healthy volunteers.

Condition

- Autoimmune disorders
- Bacterial infectious disorders

Synonym
inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Centre for Human Drug Research.

Intervention

Keyword: healthy volunteers, in vivo, inflammation, lipopolysaccharide

Outcome measures

Primary outcome

-Relationship LPS dose - inflammatory response:

Hs-CRP, cytokine panel (TNF-alpha among others, t.b.d.).

-Relationship with other systemic responses:

Coagulation: aPTT, PT.

-Tolerance/paralysis of the immune system after in vivo LPS administration:

TNF-alpha release after ex vivo whole blood LPS challenge.

-Renal damage:

KIM-1, NAG, alpha-GST, beta 2 microglobulin, creatinine.

Secondary outcome

Not applicable

Study description

Background summary

Human models of systemic inflammation have been developed with the purpose to

explore the molecular mechanisms and physiological significance of the systemic inflammatory response encountered in acute as well as chronic inflammatory disease, such as sepsis, trauma, type 2 diabetes, atherosclerosis, and Alzheimer*s disease, in a controlled, standardized experimental setting. A better understanding of the underlying molecular and pathophysiological mechanisms in acute as well as in chronic inflammation, could lead to optimized prevention and treatment of these disorders, associated with morbidity and mortality. In addition, human models of systemic inflammation can be applied in clinical pharmacology studies to assess the effects of specific interventions (medicinal or non-medicinal) on the inflammatory response in non-diseased populations.

Study objective

To assess the relationship between administration of low doses of LPS (0.5, 1 and 2 ng/kg bodyweight) and the inflammatory response (cytokine levels and hs-CRP) in healthy male volunteers;

To assess the duration of tolerance/paralysis of the immune system after in vivo LPS administration, as determined by ex vivo LPS challenges;

To assess the quantitative and temporal relationship between LPS-induced inflammation and other systemic responses (e.g. coagulation);

To assess whether in vivo LPS administration results in a (temporary) alteration of renal function, by measurement of renal damage markers.

Study design

A randomized, double-blind, placebo-controlled study of ascending single low doses of LPS administered intravenously to healthy male volunteers.

Study burden and risks

Intravenous administration of LPS can lead to influenza-like symptoms (e.g. chills, headache, eye sensitivity to light, nausea, myalgia and arthralgia), increase in core temperature and pulse rate, and decline in mean arterial pressure. Most symptoms are dose-related and resolve within 2-6 hours. As with any study involving administration of exogenous substance, rare side effects cannot be excluded beforehand. Reports of a decrease in cardiac contractility have been made following administration of 4 ng/kg bodyweight

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

-Healthy male volunteers aged 18 to 40 years, inclusive, on study day 1;
-Body Mass Index (BMI) in the range of 18 to 25 kg/m2;
-No history of alcohol or elicit drug abuse;
-No history of trauma and/or surgery to spleen;
-Free from any clinically relevant febrile illness 30 days preceding study day 1;
-No use of any prescription drugs, aspirin or other non-steroid anti-inflammatory drugs, either topical or systemic;

Exclusion criteria

-Previous participation in a LPS challenge trial or prior exposure to endotoxin in an

experimental setting within 4 weeks of the anticipate exposure;
-Recent antibiotic use, operation or intervention by surgeon/dentist;
-Any active inflammatory or infectious disease (e.g. periodontitis);
-Hypertension (defined as systolic blood pressure RR > 160 mmHg or diastolic blood pressure RR > 90 mmHg, repeatedly measured after 5 minutes in resting supine position);
-Hypotension (defined as systolic blood pressure RR < 100 mmHg or diastolic blood pressure RR < 50 mmHg);
-Clinically significant abnormalities on the 12-lead ECG (QRS complex > 120 ms, PR interval > 200 ms, QTc interval > 430 ms).

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-08-2012
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	31-07-2012
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	NL40751.018.12