Explorative study to the effect of BCG booster methods on the induction of trained innate immunity

Published: 12-04-2018
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The objective of the study is to determine the effect of BCG revaccination and high dose BCG vaccination on the induction and course of innate immune memory.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON47466

Source
ToetsingOnline

Brief title
Effects of BCG booster on TI

Condition

- Immune disorders NEC
- Ancillary infectious topics

Synonym
BCG vaccine, tuberculosis vaccine

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: NWO

Intervention

Keyword: BCG vaccin, High dose BCG vaccination, Revaccination, Trained immunity

Outcome measures

Primary outcome

1. To assess the function of monocytes measured by cytokine responses after

stimulation with unrelated antigens at different timepoints

a. before and after single standard BCG vaccination

b. before and after BCG revaccination

c. before and after high dose BCG vaccination

2. To compare cytokine responses at different timepoints

a. Between standard single dose vaccination and revaccination

b. Between standard single dose vaccination and high dose vaccination.

3. To compare transcription and epigenetic profiles of monocytes before and

after BCG (re)vaccination.

Secondary outcome

Identifying SNP variants of genes relevant for innate immune function.

Cellular metabolism of peripheral monocytes

Study description

Background summary

The live attenuated vaccine Bacillus Calmette-Guérin is able to induce
non-specific beneficial effects by protection against non related infectious

diseases beyond its target disease via epigenetic modifications. However, the effect of BCG on innate immune responses wanes after three months. The development of methods to boost the effect of BCG induced trained immunity will be of great value. This study will investigate the effect of BCG revaccination, as well as high dose BCG vaccination on the induction and course of trained immunity in healthy volunteers.

Study objective

The objective of the study is to determine the effect of BCG revaccination and high dose BCG vaccination on the induction and course of innate immune memory.

Study design

This study will be a randomized placebo controlled trial. 50 healthy volunteers, aged 18-55 years, previously BCG-unvaccinated, will be randomized to receive a BCG vaccination followed by a second BCG vaccination (group 1, n= 15), placebo vaccination (vaccine diluents) followed by high dose BCG (group 2, n = 15), placebo vaccination followed by standard dose BCG (group 3, n=15)., or placebo vaccination (twice) with an interval of three months (group 4 n = 5)

Throughout the study, blood will be drawn for ex vivo restimulations at different time points to analyze changes in immune responses after BCG vaccination. The study period will last for 6 months. Measuremens will be performed in a blinded manner.

Intervention

Group 1: standard dose BCG + standard dose BCG (0,1 ml intracuteneous injection of BCG vaccin (SSI, AJ vaccines) 0.75 mg/ml)
Group 2: placebo + high dose BCG (0,1 ml intracuteneous injection of BCG vaccin (SSI, AJ vaccines), 1,5 mg/ml)
Group 3: placebo + standard dose BCG (0,1 ml intracuteneous injection of BCG vaccin (SSI, AJ vaccines), 0.75 mg/ml)
Group 4: placebo + placebo

Study burden and risks

There will be no particular benefit for participants. BCG vaccination is safe in healthy volunteers and only mild side reactions like headache or fever occur in 1 % -0.1% of vaccinated persons. BCG vaccination will result in a small scar at vaccination site. BCG vaccination can interfere with future tuberculin skin test for tuberculosis, by causing a false positive tuberculin skin test (Mantoux test). In case of future need of screening for latent tuberculosis, BCG vaccinated volunteers should be advised to be screened by other available

methods, like chest x-ray or in vitro interferon gamma release assay.

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.
Age between 18 and 55 years old.

Exclusion criteria

Medical history associated with immunological deficiency.
History of BCG vaccination.

Chronic use of systemic drugs other than oral contraceptives.
Use of NSAIDS less than 4 weeks prior to the start of the study.
For female subjects: a positive pregnancy test at screening.
Receipt of vaccination 3 months prior to the start of the study or plans to receive any other vaccination during the study period
Acute illness two weeks prior to the start of the study.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-12-2019
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	12-04-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	21-11-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL58219.091.16