Immunisation, Treatment and Controlled Human Hookworm Infection

Published: 31-10-2018
Last updated: 10-01-2025

Primary objective:* To determine the protective efficacy of repeated short term exposure to hookworm infection Secondary objectives:1. To explore the immunological response after repeated hookworm infections2. To evaluate the safety of and number of...

Ethical review	Approved WMO
Status	Completed
Health condition type	Helminthic disorders
Study type	Interventional

Summary

ID

NL-OMON46257

Source
ToetsingOnline

Brief title
ITCHHI

Condition

- Helminthic disorders

Synonym
Hookworm infection, parasitic infection

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Stichting Dioraphte

Intervention

Keyword: Hookworm, Infectious diseases, Necator americanus, Tropical medicine

Outcome measures

Primary outcome

Primary endpoints

* Comparison of average egg counts of week 12 to 16 in the challenge phase by

Kato Katz between intervention group and placebo group

Secondary outcome

Secondary endpoints

* Adverse events collected during immunization phase and after controlled human

hookworm infection.

* Humoral (antibody) and cellular immunological changes after immunization and

after controlled human hookworm infection.

Study description

Background summary

Hookworm infection affects over 450 million people worldwide. Chronic infection leads to malnutrition and iron-deficiency anaemia, particularly in children and women of child-bearing age. Unfortunately, mass drug administration, the cornerstone of hookworm control programmes, has not yet succeeded in eradicating hookworm infection due to high rates of re-infection.
Controlled human hookworm infection (CHHI) trials were initially developed as a model for to assess the beneficial effects of hookworm infection on autoimmune diseases. CHHI models are also being developed to assess vaccine efficacy. Another advantage of the controlled human hookworm infection model is its unique possibility to study immunologic responses in a highly controlled setting, thereby adding valuable knowledge of the host immune responses to infection. Little is known about the factors influencing host protection against repeated infection. In natural infection the human host develops an inadequate immune response to infection. This may be caused by the

down-regulatory effect of the Th2 response caused by the adult worms in the intestine. In animal models, short-term infections and infections with radiation-attenuated larvae that do not develop into adult worms have shown to induce protection against subsequent challenge. A similar model in humans, using short-term infections abrogated by treatment can add valuable knowledge about the initial immune response against hookworm infection which may in turn aid in developing new vaccines.

Study objective

Primary objective:
* To determine the protective efficacy of repeated short term exposure to hookworm infection
Secondary objectives:
1. To explore the immunological response after repeated hookworm infections
2. To evaluate the safety of and number of events after short term hookworm infections

Study design

This study is a double-blind, randomised placebo-controlled trial.

Intervention

Twenty-four volunteers are randomized in a 2:1 ration to the intervention group or placebo-group.
Immunization phase: In the intervention group, volunteers will receive three infections with 50 L3 larvae of Necator americanus at a 3-week interval. Volunteers in the placebo group will receive a mock infection with water to maintain blinding. Two weeks after each infection all volunteers will be treated with albendazole.
Challenge phase: Five weeks after the last treatment, all volunteers will undergo controlled human hookworm infection with 50 L3 larvae and will be followed for 16 weeks. At week 16 all volunteers will be treated with albendazole, except a subset of a maximum of four volunteers who will be asked to remain as donor for future trials. After treatment volunteers are followed to ensure treatment was effective.

Study burden and risks

Burden: Volunteers are required to visit the study centre for eight visits during the immunization phase and for twenty visits during the challenge phase. The number of follow-up visits is the same for all groups. The amount of blood collected per volunteer will be a maximum of 500 mL per 16 weeks. Faecal samples will be taken every two to four weeks during the immunisation phase and weekly in the challenge phase. Physical examinations will be performed when

clinically indicated and subjects will be asked to complete a diary of adverse events on a daily basis during the challenge phase. Volunteers may experience itching at the infection site and can experience gastro-intestinal side effects from two to four weeks after the challenge.
Risks: Volunteers will be exposed to larval inoculum two or five times depending on group allocation. Risks related to infection include skin rash and gastro-intestinal symptoms. Symptoms are reversible and can be treated if necessary. In a previous trial one in eight volunteers suffered from severe abdominal pain necessitating earlier treatment, four in eight volunteers did not experience any or only mild adverse events. In natural infection the main risks are iron-defiency anaemia and protein loss, however in CHHI with healthy volunteers this is not expected. Volunteers are treated four times with albendazole during the course of the trial. Possible side effects posing risk to volunteers related to albendazole treatment are headache, dizziness, reversible alopecia and elevated liver enzymes. Clearance of infection is confirmed by faecal Kato-Katz and qPCR. Volunteers are followed and if necessary re-treated until the infection is completely cleared. No long-term risks are expected.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. Subject is aged * 18 and * 45 years and in good health.
2. Subject has adequate understanding of the procedures of the study and agrees to abide strictly thereby.
3. Subject is able to communicate well with the investigator and is available to attend all study visits.
4. Subject agrees to refrain from blood donation to Sanquin or for other purposes throughout the study period.
5. For female subjects: subject agrees to use adequate contraception and not to breastfeed for the duration of study.
6. Subject agrees to refrain from travel to a hookworm endemic area during the course of the trial.
7. Subject has signed informed consent.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1. Any history, or evidence at screening, of clinically significant symptoms, physical signs or abnormal laboratory values suggestive of systemic conditions, such as cardiovascular, pulmonary, renal, hepatic, neurological, dermatological, endocrine, malignant, haematological, infectious, immune-deficient, psychiatric and other disorders, which could compromise the health of the volunteer during the study or interfere with the interpretation of the study results. These include, but are not limited to, any of the following:
* positive HIV, HBV or HCV screening tests;
* the use of immune modifying drugs within three months prior to study onset (inhaled and topical corticosteroids and oral anti-histamines exempted) or expected use of such during the study period;
* having one of the following laboratory abnormalities: ferritine <10ug/L, transferrine <2.04g/L or Hb <6.5 mmol/L for females or <7.5 mmol/L for males.
* history of malignancy of any organ system (other than localized basal cell carcinoma of the skin), treated or untreated, within the past 5 years;
* any history of treatment for severe psychiatric disease by a psychiatrist in the past year;
* history of drug or alcohol abuse interfering with normal social function in the period of one year prior to study onset;

* inflammmatory bowel syndrome;
* regular constipation, resulting in bowel movements less than three times per week.
2. Known hypersensitivity to or contra-indications for use of albendazole, including co-medication known to interact with albendazole metabolism (e.g. carbamazepine, phenobarbital, phenytoin, cimetidine, theophylline, dexamethasone).
3. Known allergy to amphotericin B or gentamicin.
4. For female subjects: positive urine pregnancy test at screening.
5. Positive faecal qPCR for hookworm at screening, any known history of hookworm infection or treatment for hookworm infection.
6. Being an employee or student of the department of Parasitology of the LUMC.
7. Current or past scars, tattoos, or other disruptions of skin integrity at the intended site of larval application.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	09-11-2018
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	31-10-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

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	NL66725.058.18
Other	volgt

Study results

Date completed:	02-09-2019
Results posted:	15-10-2020
Actual enrolment:	23

First publication
01-01-1900