Maintaining Controlled Human Hookworm Infection Model studies at Leiden University Medical Centre

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24634

Source
NTR

Brief title
CHHIL2

Health condition

hookworm

Sponsors and support

Primary sponsor: LUMC (Prof. M. Yazdanbakhsh)
Source(s) of monetary or material Support: LUMC & NWO-WOTRO

Intervention

Outcome measures

Primary outcome

Primary objectives:
- To establish two hookworm-infected donors to set up the controlled human hookworm infection model in Gabon

- To study early-phase immune responses to hookworm exposure during the first four weeks after challenge

Secondary outcome

Exploratory objectives:
- To describe the number of adverse events following single exposure to hookworm larvae

Study description

Background summary

Rationale: A safe and efficacious vaccine against hookworm is urgently needed. Animal models to test vaccines are not available, therefore controlled human hookworm infection (CHHI) studies can be of great value to speed up vaccine development. Because immune responses of hookworm-endemic populations clearly differs from naïve populations, we have recently embarked on a project to transfer the hookworm controlled human infection model to our research collaborators at CERMEL. In order to train and certify staff at CERMEL in Gabon, we will need continued access to hookworm eggs and larvae. Once training has been completed, the Gabonese team will establish chronic donors with a (local) Gabonese hookworm strain. Should there be technical difficulties with establishing chronic donors and obtaining infectious larvae, the hookworm donors in Leiden will serve as a backup to provide infectious larvae. Moreover, we will use this study to further elucidate early phase immune responses to hookworm exposure.
The aim of this study therefore is to recruit healthy individuals to become hookworm donors for future CHHI studies at the LUMC and Gabon and to study early-phase immune responses.

Objectives:
Primary objectives:
- To establish two hookworm-infected donors to set up the controlled human hookworm infection model in Gabon
- To study early-phase immune responses to hookworm exposure during the first four weeks after challenge

Exploratory objectives:
- To describe the number of adverse events following single exposure to hookworm larvae

Study design: An open-label intervention study

Study population: Hookworm-naïve, 18-45 year male adults

Intervention: Four participants will be exposed to 50 Necator americanus (Na) larvae at week 0. Weekly follow up site visits will take place until week 4 after infection. Afterwards weekly follow up phone calls, will take place to collect adverse events until 12 weeks after the first infection. At week 12 and 13, participants will provide a total of four stool samples for egg

quantification. Based on these results, two participants will be treated at week 14, while the other two will remain infected and become donors for the rest of the study. Those treated early will come to evaluate treatment at week 15 and week 17. After week 14 donors will regularly (roughly 5-10 times/year) be asked to donate faeces (= on demand donation). After 2 years, or if volunteers decide to withdraw earlier, treatment with albendazole will be initiated. Treatment of donors will be evaluated at 1 and 3 weeks after dosing.

Main study parameter/endpoint:
- Detection of hookworm eggs by faeces microscopy (Kato-Katz) at week 12 and 13 post-infection.
- Humoral and cellular immunological changes in the first month after exposure to hookworm

Exploratory study parameters:
- Number of adverse events following exposure to hookworm larvae

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
Benefits: There is no benefit of participation in the trial for the individual volunteers. Therefore the risk and discomfort of participation for individual volunteers should be carefully weighed against the scientific advantage of the controlled human Na infection model, in particular for vaccine and drug development.
Burden and risks: The number of study visits varies between participants. The two volunteers that become chronic donors visit the trial centre at least 12 times, excluding on demand donations. Those that are treated early visit the centre 11 times. Check-up visits last approximately 15 minutes. The controlled human hookworm infection visits last two hours. During check-up visits blood is drawn. Volunteers are required to regularly collect faeces samples.
In natural infection the main risks of hookworm infection are iron-deficiency anaemia (IDF) and protein losses. This, however, has not been observed in healthy volunteers in previous controlled human hookworm trials. The risks to volunteers pertain to exposure to larval inoculum and treatment with albendazole. Adverse events expected after infection include skin reactions (rash and itching) and gastro-intestinal symptoms, such as diarrhea and abdominal pain. Skin rash may occur immediately after infection. The duration of the rash in volunteers exposed to 1x 50 larvae ranges between 0 and 34 days (median: 27 days). Itching can also occur from the moment of infection and typically lasts for three days (median duration), with a maximum of 23 days. Volunteers with a darker skin may experience depigmentation or hyperpigmentation at the site of larval inoculation. This may result in permanently visible lesions of approximately one millimetre. Our experience in previous CHHI infections is that nearly all volunteers develop gastro-intestinal adverse events, but that there is great interindividual variation in the severity of these gastro-intestinal adverse events. Previously, we did not find a relationship between infectious dose and gastrointestinal events. Treatment with albendazole has shown to effectively resolve the symptoms in the previous trials. Side effects of albendazole may include headache, dizziness, transient alopecia and elevated liver enzymes. Liver enzymes will be checked after albendazole treatment. In longer administration of albendazole neutropenia has been described, however this is unlikely due to the short course given in this trial (3 days). Volunteers in the study will be exposed to risks associated with chronic hookworm infection that include iron deficiency,

iron-deficiency anaemia, and chronic gastrointestinal symptoms, (i.e. flatulence, abdominal pain, diarrhea, nausea, vomiting, abdominal bloating). Previously, we found that our chronic donors (n=7) are asymptomatic after 16 weeks and do not develop anaemia. Donors also visit the trial centre one year after infection for follow-up.
Group-relatedness: Not applicable

Study objective

N/A

Study design

All participants: screening, week 0-13
Non-donors: week 14, 15, 17
Donors: week 52, 101, 102, 104 and 'on demant donations' (ODD)

Intervention

50L3 Necator americanus larvae

Contacts

Public
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Meta Roestenberg

071-5262102
Scientific
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Eligibility criteria

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 is male.

3. Subject has adequate understanding of the procedures of the study and agrees to abide strictly thereby.
4. Subject is able to communicate well with the investigator and is available to attend all study visits.
5. Subject agrees to refrain from blood donation to Sanquin or for other purposes throughout the study period.
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: ferritin <10ug/L, transferrin <2.04g/L or Hb <7.5 mmol/L.
- 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;
- inflammatory 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. Positive faecal qPCR for hookworm at screening, any known history of hookworm infection or treatment for hookworm infection.
5. Being an employee or student of the department of Parasitology of the LUMC.
6. 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:	Other
Allocation:	Non controlled trial

Control: N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	04-04-2021
Enrollment:	4
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	06-01-2021
Application type:	First submission

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
NTR-new	NL9178
Other	METC-Leiden-Den Haag-Delft : METC-LDD: P20.100

Study results