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Effects of filarial parasite infection on type 2 diabetes

Submission date	Recruitment status	[X] Prospectively registered
27/11/2019	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
02/12/2019	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
23/01/2025	Infections and Infestations	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Type 2 diabetes is a growing challenge for health care systems in Africa. In Cameroon, more than half a million patients suffer from diabetes. Diabetes is one of the major causes for global mortality, morbidity and health care expenditures, which will aggravate especially in Africa, where around 67% of diabetic subjects are undiagnosed and it is predicted that until 2035, the number of diabetes patients will more than double.
Filariasis is a parasitic disease caused by an infection with roundworms of the Filarioidea type. These are spread by blood-feeding diptera such as black flies and mosquitoes. This disease belongs to the group of diseases called helminthiases. Eight known filarial nematodes use humans as their definitive hosts.
It is important to elucidate the effect of helminth infections and their impact on diabetes. Therefore this study will investigate the impact of filarial infections on immune and metabolic profiles to predict the risk to develop diabetes.

The objectives of the study are
1. To investigate the association between human filarial infections and other diseases such as diabetes, high blood pressure etc.
2. To elucidate whether treatment against filariae affects other diseases such as diabetes, high blood pressure etc.

Who can participate?
To participate in this research, participants must be between 18 and 60 years of age and their body mass index (BMI) should be 30 or greater or alternatively below 25. We will screen for O. volvulus, M. perstans, Loa Loa and include patients that are either positive for one of those helminth infections or lack helminth infections (endemic controls). The study participants should not have clinical signs of tuberculosis, HIV, any known chronic disease.

What does the study involve?
Onchocerca volvulus, Mansonella perstans infected participants will receive 200 mg of doxycycline daily for 6 weeks, which will eliminate the filarial infection. Patients co-infected with Onchocerca and Mansonella will also be treated with 200 mg of doxycycline daily for 6 weeks. As L. loa does not contain Wolbachia endosymbionts, doxycycline treatment will not affect L. loa co-

infection. In addition, onchocerciasis patients, M. perstans infected patients, and L. loa infected individuals and endemic controls will receive a single dose of 400 mg albendazole every 3 months with a total of four treatments for the elimination of soil-transmitted helminths.
Blood sample collection will occur at baseline, 12 months and 24 months. For the determination of intestinal helminths, the researchers will additionally require stool samples at baseline, follow-up, 12 months and 24 months. To determine Onchocerca volvulus infection and microfilarial density, the researchers will perform two skin snips (a superficial cut of the skin) the size of a fingertip at baseline, 12 months and 24 months.

What are the possible benefits and risks of participating?
Benefits: treatment of the infection
Risks: We do not expect any major risks, but the patient could feel some discomforts due to blood drawing.

Where is the study run from?
District de Sante de Manjo in Cameroon

When is the study starting and how long is it expected to run for?
January 2020 to December 2026

Who is funding the study?
German Research Foundation

Who is the main contact?
1. Dr Marc Hübner (scientific)
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
FIMMIP HU 2144/3-1

Study information

Scientific Title
Impact of human filarial infections on the metabolic and immunological profile in type 2 diabetes

Acronym
FIMMIP

Study objectives
1. Immunomodulation by infections with the filarial nematodes Mansonella perstans and Onchocerca volvulus improves the glycaemic and metabolic parameters.
2. Anti-filarial therapy has adverse effects on the metabolic and immunological profile of obese and lean filariasis patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 10/10/2017, changes approved 22/12/2021, Comite National D´ethique De La Recherche Pour La Sante Humaine (National committee on the ethics of research for human health, Medical research Station, P.O. Box 55, Kumba, Cameroon; +237 33354231;

cnethique_minsante@yahoo.fr) ref: No2019/03/1153CE/CNERSH/SP
2. Approved 20/03/2018, changes approved 13/12/2021, Rheinische Friedrich-Wilhelms-Universität, Medizinische Fakultät, Ethik Kommission (Ethics commission of the faculty of medicine, Building 13, Room 2G 029, Rheinische Friedrich-Wilhelms-Universität, Venusberg-Campus 1, Biomedizinisches Zentrum, Bonn, Germany; +49-228-287-5193; ethik@uni-bonn.de), ref: 046/18

Study design
Interventional controlled open-label pilot trial

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Human filarial infection and type 2 diabetes

Interventions
Current interventions as of 24/01/2022:
1. Patients infected with M. perstans:
Patients will be divided into lean (BMI <25) and obese (BMI ≥ 30). All volunteering patients will receive the interventional treatment 200 mg of doxycycline daily for 6 weeks. All volunteering patients who refuse treatment will serve as an untreated control. All participants will receive a single dose of 400 mg albendazole every 3 months with a total of four treatments for the elimination of soil-transmitted helminths. Treatment of L. loa co-infected individuals with doxycycline and albendazole does not kill the adult L. loa filariae.

2. Patients infected with O. volvulus:
Patients will be divided into lean (BMI <25) and obese (BMI ≥ 30). All volunteering patients will be treated with interventional treatment 200 mg of doxycycline daily for 6 weeks. All volunteering patients who refuse treatment will serve as an untreated control. All participants will receive a single dose of 400 mg albendazole every 3 months with a total of four treatments for the elimination of soil-transmitted helminths. Treatment of L. loa co-infected individuals with doxycycline and albendazole does not kill the adult L. loa filariae.

3. Endemic Normals (not infected with M. perstans or O. volvulus or any other helminths or disease mentioned in the exclusion criteria).
Participants will be divided into lean (BMI <25) and obese (BMI ≥ 30). All volunteering participants will be treated with a single dose of 400 mg albendazole every 3 months with a total of four treatments for the elimination of soil-transmitted helminths.

4. Loa loa infected
Participants infected with Loa loa will receive a single dose of 400 mg albendazole every 3 months with a total of four treatments for the elimination of soil-transmitted helminths. Treatment of L. loa co-infected individuals with albendazole does not kill the adult L. loa filariae.

Blood sample collection will occur at baseline, 12 months and 24 months. For the determination of intestinal helminths the researchers will additionally require stool samples at baseline, follow-up, 12 months and 24 months. To determine Onchocerca volvulus infection and microfilarial

density, the researchers will perform two skin snips (a superficial cut of the skin) the size of a fingertip at baseline, 12 months and 24 months.

All subjects will be followed up 12 and 24 months post-treatment and the immunological and disease-related parameters will be analyzed

Previous interventions:

1. Patients infected with M. perstans:
Patients will be divided into lean (BMI <25) and obese (BMI ≥ 30). From each group half of the patients will receive the interventional treatment (200 mg of doxycycline daily for 6 weeks) and the other half will be the control. (Participants of this study will obtain an individual code and the code will be referred to Bonn, Germany, where we will randomly allocate half of the participants of group 1 to doxycycline treatment, without knowing any details of the participants. The individual codes of the selected participants for doxycycline therapy will then be forwarded to our partners in Cameroon.)

2. Patients infected with O. volvulus:
Patients will be divided into lean (BMI <25) and obese (BMI ≥ 30). All volunteering patients will be treated with four rounds of 150µg/kg ivermectin (Mectizan) in 3-month intervals in the process of a community-based mass drug administration (MDA). Patients who refuse treatment will serve as an untreated control.

3. Endemic Normals (not infected with M. perstans or O. volvulus or any other helminths or disease mentioned in the exclusion criteria).
Patients will be divided into lean (BMI <25) and obese (BMI ≥ 30). All volunteering patients will be treated with four rounds of 150 µg/kg ivermectin (Mectizan) in 3-month intervals in the process of a community-based mass drug administration (MDA). Patients who refuse treatment will serve as an untreated control.

In addition: 400 mg albendazole every 3 months with a total of four treatments for groups 1, 2 and 3.

Blood sample collection will occur at baseline, 12 months and 24 months. For the determination of intestinal helminths we will additionally require 3 stool samples at baseline, 12 months and 24 months. To determine Onchocerca volvulus infection and microfilarial density, we will perform two skin snips (a superficial cut of the skin) the size of fingertip at baseline, 12 months and 24 months.

All subjects will be followed up 12 and 24 months post-treatment and the immunological and disease-related parameters will be analyzed

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Doxycycline, ivermectin, albendazole

Primary outcome(s)

Measured using blood test at baseline and follow-up (12 and 24 months):
1. Fasting glucose measured by autoanalzyer
2. HbA1C measured by Reflotron; updated 24/01/2022: HbA1C measured by HumaStar200
3. Serum insulin measured by ELISA
4. HOMA-IR measured by the homeostasis assessment (HOMA) model (fasting insulin (mIU/ml) × fasting)

Key secondary outcome(s))
Measured using blood test at baseline and follow-up (12 and 24 months):
1. Alpha-2- macroglobulin, C-peptide, TNF, IL-6, IL-10, adipokines, gut hormones, IgG subtypes, IgE, IgA (by ELISA or multiplex)
2. Total and differential cell counts (by automated differential cell counter)
3. Quantification of naïve, effector and central memory CD4+ and CD8+ T cells, regulatory T cells (Tregs), NK cells, dendritic cells (DC) and B cells in whole blood, cytokine producing T cells (by flow cytometry)
4. Lipid profile (total, HDL and LDL cholesterol, triglycerides – by autoanalyzer and Friedewald equation for LDL); AST, ALT, ALP, GGT, serum creatinine, urea, urine albumin, (by autoanalyzer)
5. Body weight, BMI, adipose tissue and muscle ratio (by weight scale body fat analyzer)
6. Blood pressure (blood pressure measurement device)
7. Waist and hip circumference (measuring tape)
8. Measured at baseline only: Questionnaire on medical history, dietary and physical behavior

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 24/01/2022:
1. Willingness to participate in the study as evidenced by signing the Informed consent form
2. Participants will be male and female between 18-60 years old
3. BMI equal to or above 30 or below 25
4. Body weight >40 kg
5. Last intake of ivermectin at least 4 months ago
6. Last intake of anti-filarial antibiotic treatment more than 12 months ago
7. Resident in an endemic area for at least 5 years
8. O. volvulus patients with microfilariae skin snip positive and PCR positive for O. volvulus
9. M. perstans patients positive for microfilariae
10. PCR endemic controls, judged by absence of microfilariae, palpable onchocercoma, PCR negative for M. perstans and O. volvulus
11. Individuals should be free of other helminth infections and possess normal eosinophil frequencies (1-4%) and IgE levels (<100 IU/ml)
12. Good general health without any clinical condition requiring long-term medication
13. Normal white blood cell counts (3.5-11.3 x 10^3/µl)

Previous inclusion criteria:
1. Willingness to participate in the study as evidenced by signing the Informed consent form
2. Participants will be male and female between 18-45 years old
3. BMI equal to or above 30 or below 25
4. Body weight >40 kg
5. Last intake of ivermectin at least 4 months ago

6. Last intake of anti-filarial antibiotic treatment more than 12 months ago
7. Resident in an endemic area for at least 5 years
8. O. volvulus patients with microfilariae skin snip positive and PCR positive for O. volvulus
9. M. perstans patients positive for microfilariae
10. PCR Endemic controls, judged by absence of microfilariae, palpable onchocercoma, PCR negative for M. perstans and O. volvulus.
11. Individuals should be free of other helminth infections and possess normal eosinophil frequencies (1-4%) and IgE levels (<100 IU/ml).
12. Good general health without any clinical condition requiring long-term medication
13. Normal white blood cell counts (4.4-11.3 x 10^3/µl)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Total final enrolment
2171

Key exclusion criteria
1. Pregnancy (dipstick pregnancy test)
2. Lactating mothers
3. Last intake of ivermectin (IVM) less than 4 months ago
4. Intake of anti-filarial antibiotic treatment (tetracycline) less than 12 months ago
5. Evidence of tuberculosis (clinical aspects)
6. Evidence of clinical aspects of HIV infection
7. Evidence/previous diagnosis of chronic diseases (urolithiasis, liver cirrhosis, congestive heart failure, chronic lung diseases, chronic infections other than filariae, viral hepatitis)
8. Evidence of autoimmune diseases (except for diabetes) and allergies
9. Evidence of acute infection (haematuria, cough, fever). Evidence of clinically significant neurological, cardiac, pulmonary, metabolic, rheumatologic or renal disease as far as can be assessed by history of individuals, physical examination, and/or laboratory examinations
10. Childbearing potential and not willing or able to use methods to prevent pregnancy for the entire treatment duration in addition to hormonal contraception (e.g. condoms) unless surgically sterilized/ hysterectomized or any other criteria considered sufficiently reliable by the investigator.
11. Behavioural, cognitive or psychiatric disease that in the opinion of the trial clinician affects the ability of the participant to understand and cooperate with the study protocol

Added 24/01/2022:
12. Laboratory values that will lead to exclusion:
12.1. Haemoglobin <8 g/dl
12.2. Neutrophil count <500/µl*
12.3. Platelet count <100,000/µl
12.4. Creatinine >2 times upper limit of normal
12.5. AST (GOT) >2 times upper limit of normal
12.6. ALT (GPT) >2 times upper limit of normal
12.7. γ-GT >2 times upper limit of normal

Date of first enrolment
01/01/2020

Date of final enrolment
30/06/2023

Locations

Countries of recruitment
Cameroon

Study participating centre
District de Sante de Manjo in Cameroon
Manjo
Cameroon
N/A

Sponsor information

Organisation
University of Buea, Faculty of Science, Department of Microbiology and Parasitology

ROR
https://ror.org/041kdhz15

Funder(s)

Funder type
Research organisation

Funder Name

Deutsche Forschungsgemeinschaft

Alternative Name(s)
German Research Association, German Research Foundation, Deutsche Forschungsgemeinschaft (DFG), DFG

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		02/06/2023	05/06/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes