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Anti-wolbachial therapy with doxycycline to ameliorate filaricele pathology

Submission date	Recruitment status	[_] Prospectively registered
31/05/2010	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/07/2010	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
08/07/2010	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
1/81306 extension

Study information

Scientific Title
Anti-wolbachial therapy with doxycycline to ameliorate filaricele pathology: a randomised, double-blind, placebo-controlled trial

Study objectives
1. To assess the possibility of using the combination of doxycycline treatment and ultrasound-guided aspiration of hydrocele fluid to replace or supplement the current hydrocelectomy strategy.
2. To explore the possibility to differentiate between hydrocele and chylocele by ultrasonography (USG).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical clearances have been obtained from the Committee on Human Research Publication and Ethics, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana (approved April 29th, 2010) and from the Ethical Committee, University Clinic Bonn, Faculty of Medicine, Bonn, Germany (approved March 8th, 2010).

Primary study design
Interventional

Study design
Randomised double blind placebo controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Lymphatic filariasis (Wuchereria bancrofti)

Interventions
The participants will be randomised and assigned to one of two treatment regimens:
1. 6 weeks doxycycline (2 x 100 mg/day) (n = 33)
2. 6 weeks placebo matching doxycycline (2 capsules/day) (n = 33)

Volunteers for this study are recruited based on the inclusion and exclusion criteria and treated directly in their villages (Ahanta West district, Ghana). The study-drugs will be distributed ad personam by the research staff and drug intake monitored on a daily basis for 6 weeks.
All participants will undergo ultrasound-guided aspiration 4 months after treatment onset. Two experienced MDs (urologist and ultrasonographer) will perform the aspiration together under aseptic conditions in a hospital. To avoid traumata during aspiration (lesions of the testis or intra-scrotal vessels) a disposable needle guide will be affixed to the ultrasound transducer by a clamp. This device will help the urologist to aid in positioning the needle to impede that the needle/drainage tube gets too close to the testis and scrotal vessels and therefore prevents unwanted bleeding or lesions of the tunica vaginalis parietalis and visceralis and the testis. Skin disinfectant and sterile ultrasound gel will be used to prevent infection due to exogenous bacteria. The total amount of fluid surrounding the testis will be obtained. 24 hours after aspiration participants will be visited and scanned again for safety reasons to make sure that no bleeding or infection occurred. In case of any aspiration related problem, the responsible urologist and MD will care for the patient until resolution. The patient will receive appropriate treatment, i.e. analgesic drugs, antibiotics, if necessary.
The total duration of follow-up for both arms of our trial is 12 months after the start of drug administration.

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Intervention Type
Other

Phase
Phase IV

Primary outcome(s)
Improvement of filaricele size (stage) between study onset (pre-treatment) and 8 months after aspiration (12 months after study onset). Improvement is defined as pre-treatment stage of hydrocele minus one stage (minimum) 8 months after aspiration. Hydrocele stage is determined according to Debrah et al.,2007.

Key secondary outcome(s)
1. Improvement of filaricele size (stage) between study onset (pre-treatment) and pre-aspiration (time point 4 months after doxycycline/placebo treatment) as well as 3 months after aspiration (7 months after study onset)
2. Improvement of filaricele size (stage) between pre-aspiration (4 months after study onset) and 3 and 8 months after aspiration (7 and 12 months after study onset)
3. Curative effect of the combined drug and aspiration treatment, measured at 3 and 8 months after aspiration (i.e. 7 and 12 months after drug treatment onset). A curative effect is defined as no fluid accumulation (no relapse after aspiration)
4. Reduction of supra-testicular lymphatic vessel dilation between pre-treatment and pre-aspiration as well as 3 and 8 months after aspiration (7 and 12 months after start of treatment)
5. Proof or rejection that improvement of hydrocele stage correlates with increase of immunosuppressive markers e.g. TGF, IL-10, lower levels of inflammatory cytokines e.g. IL-4, IL-6, IL-12, IL-17, INFγ, TNF and decrease of angiogenic parameters, e.g. VEGFs, measured in blood samples pre-treatment, pre-aspiration as well as 3 and 8 months after aspiration (7 and 12 months after start of treatment)
6. Proof or rejection that improvement of hydrocele stage correlates with increase of immunosuppressive markers e.g. TGF, IL-10, lower levels of inflammatory cytokines e.g. IL-4, IL-6, IL-12, IL-17, INFγ, TNF and decrease of angiogenic parameters, e.g. VEGFs, measured in hydrocele fluid obtained during aspiration. Clinical findings at 3 and 8 months after aspiration

will be assessed and correlated with results of the aspirated fluid
7. Proof or rejection that USG is able to differentiate chylocele (EDH) from hydrocele (EFH) based on correlation of biochemical markers such as chylomicrons, lipoproteins, cytokines, with ultrasonographical findings

Completion date
31/05/2012

Eligibility

Key inclusion criteria
1. Men between 18-55 years old
2. Good general health, without any clinical condition requiring long-term medication and with normal renal and hepatic laboratory profiles
3. Body weight > 40 kg
4. Presence of hydrocele stage 2 or 3, detected by ultrasound (as described in Debrah et al., 2007)
5. Willingness to participate in the study as evidenced by signing of the informed consent document (written or thumb print)
6. Resident in the endemic area for 5 years or more

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Male

Key exclusion criteria
1. Known intolerance to the study drug doxycycline
2. History of a severe allergic reaction or anaphylaxis
3. History of alcohol or drug abuse
4. Evidence of clinically significant neurological, cardiac, pulmonary, hepatic, rheumatologic, metabolic or renal disease as far as it can be assessed by history of participants, physical examination, and/or laboratory examinations including blood and urine analyses
5. Laboratory evidence of liver disease (alanine aminotransferase [ALT], gamma-glutamyl transferase [gamma-GT] greater than 1.25 times the upper limit of normal results given by the dipstick test manufacturer, Roche)
6. Laboratory evidence of renal disease (serum creatinine greater than 1.25 times the upper limit

of normal results given by the dipstick test manufacturer, Roche)
7. Laboratory evidence of diabetes (urine dipstick chemistry)
8.Behavioural, cognitive, or psychiatric disease that, in the opinion of the trial clinician, affects the ability of the participant to understand and comply with the study
9. Severe asthma or respiratory disease (evidenced by a past emergency room visit or hospitalization)
10. Participation in other drug trials concurrent with this study
11. Any other condition that, in the opinion of the investigator (trial clinician), would risk the safety or rights of a participant in the trial or would render the subject unable to comply with the protocol

Date of first enrolment
01/05/2010

Date of final enrolment
31/05/2012

Locations

Countries of recruitment
Germany

Ghana

Study participating centre
Institute of Medical Microbiology, Immunology and Parasitology
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Sponsor information

Organisation
Volkswagen Foundation (VolkswagenStiftung) (Germany)

ROR
https://ror.org/03bsmfz84

Funder(s)

Funder type
Charity

Funder Name
Volkswagen Foundation (VolkswagenStiftung) (Germany) (ref: 1/81 306 extension)

Alternative Name(s)
VolkswagenStiftung, The Volkswagen Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary