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The role of isoniazid medication in preventing progression to active tuberculosis disease in persons with latent tuberculosis: The effect on the body's immune system

Submission date
17/09/2015

Recruitment status
No longer recruiting

Registration date
30/09/2015

Overall study status
Completed

Last Edited
26/10/2015

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Tuberculosis (TB) is a highly contagious bacterial infection. It is generally spread by breathing in tiny droplets released into the air by an infected person coughing or sneezing. TB usually affects the lungs, but it can also affect other areas of the body such as the bones, brain and kidneys. When a person is suffering from active TB, they are visibly unwell and can spread the infection to others. Many people however have latent TB, where the bacteria remain in an inactive state in the body. A person with latent TB has no symptoms and cannot spread the infection to others. Without treatment, the infection can become active at any time, and so monitoring people with latent TB is a vital part of controlling the spread of TB in general. Isoniazid is an antibacterial medication which has been used for many years to treat active TB infections. This drug is also commonly used to prevent active TB developing in people who have come into contact with an infected person. The aim of this study is the way that isoniazid preventative treatment (IPT) affects the body in people with latent TB, and if it can increase immunity to TB in general.

Who can participate?
Healthy people above 5 years of age, who are living with someone diagnosed with active TB.

What does the study involve?
Participants are randomly allocated into two groups. The first group receive isoniazid tablets for six months as well as attending monthly clinic visits. The second group attend monthly clinic visits only. All participants are tested for latent TB infection using a blood test at the start of the study, and then again after six months.

What are the possible benefits and risks of participating?
Participants benefit from receiving a free blood test to screen them for TB and HIV, as well as education about the medication they may be taking so that they are fully prepared for any possible side effects. Risks of participating are minimal, including pain or bruising from blood tests, as well as finding the interviews tiring.

Where is the study run from?
1. Kitebi Health Center III (Uganda)
2. Kisenyi Health Center IV (Uganda)

When is the study starting and how long is it expected to run for?
May 2011 to January 2012

Who is funding the study?
1. Seventh Framework Programme (Belgium)
2. Wellcome Trust (UK)

Who is the main contact?
Dr Irene Andia-Biraro

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title

The effect of isoniazid preventive therapy on immune responses of household contacts with latent tuberculosis infection

Study objectives
Household contacts of active tuberculosis patients with latent tuberculosis infection would present with mixed Th1/Th2 cytokine profiles and treatment of the latently infected people with isoniazid would reverses the immune equilibrium from Th2 responses back to Th1 immune dominance.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. The Makerere University College of Health Sciences Ethical Review Board, 10/09/2009, ref: 2009-140
2. Uganda National Council for Science and Technology, 16/09/2009, ref: HS 676

Study design
Redomised controlled trial nested within a cohort study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Latent tuberculosis infection

Interventions
Household contacts that were eligible for the study were randomized to receive either isoniazid preventive therapy (IPT) and monthly visits or monthly visits only. Household contacts in the IPT arm were offered self-administerd isoniazid (5mg/kg to a max of 300mg) plus pyridoxine 25mg daily for six months.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Isoniazid

Primary outcome measure
1. Net cytokine responses measured from Quantiferon supernatants using an 11-analyte Bio-Plex human cytokine bead array consisting of IFN-γ, IL-2, TNF-α, IL-4, IL-5, IL-13, IL-10, IL-17a, IL-17f, IL-21, and IL-22, among the household contacts at the end of six-months follow up
2. Mtb specific antibody concentrations to purified protein derivative (PPD), culture filtrate protein 10 (CFP-10), early secreted antigenic target 6 (ESAT-6) antigens using an in-house IgG ELISA assay, among the household contacts at the end of six-months follow up

Secondary outcome measures
1. The spontaneous cytokine responses measured from Quantiferon supernatants using an 11-analyte Bio-Plex human cytokine bead array consisting of IFN-γ, IL-2, TNF-α, IL-4, IL-5, IL-13, IL-10, IL-17a, IL-17f, IL-21, and IL-22 at the end of six-months follow up
2. Any side effects due to IPT found during clinical assessment at each monthly clinic visit or reported as they occur
3. Any changes in TST and QFN test reactions between baseline and at the end of six-months follow up
4. Incidence of active TB acquired during the course of the six-months follow up

Overall study start date
01/03/2009

Completion date
20/10/2014

Eligibility

Key inclusion criteria
Household contacts exposed to patients with sputum smear positive tuberculosis that are:
1. Above the age of 5 years
2. HIV negative
3. Tested positive on both the tuberculin skin test and the QuantiFERON®-TB Gold In-Tube® test (Cellestis GmbH (Europe), Hannover, Germany; QFN)

Participant type(s)
Other

Age group
Mixed

Sex
Both

Target number of participants
The target number is 145

Key exclusion criteria
Household contacts excluded if they have:
1. Signs and symptoms of active tuberculosis

2. Liver disease
3. Epilepsy

Date of first enrolment
01/05/2011

Date of final enrolment
31/01/2012

Locations

Countries of recruitment
Uganda

Study participating centre
Kitebi Health Center III
Kampala
Uganda
041

Study participating centre
Kisenyi Health Center IV
Kampala
Uganda
041

Sponsor information

Organisation
College of Health Sciences, Makerere University

Sponsor details
P. O. Box 7072
Kampala
Uganda
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Sponsor type
University/education

Website
http://.chs.mak.ac.ug

ROR
https://ror.org/03dmz0111

Funder(s)

Funder type
Research organisation

Funder Name
Wellcome Trust Strategic Award through the Makerere University-Uganda Virus Research Institute Infection and Immunity Research Training Programme (MUII)

Funder Name
Seventh Framework Programme

Alternative Name(s)
EC Seventh Framework Programme, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
The manuscript of the trial findings are about to be published and the journal required the study to be registered before it could publish the work.

Intention to publish date
31/10/2015

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Results article	results	22/10/2015	Yes	No