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Prevention of infection in patients with cirrhosis with probiotic Lactobacillus casei Shirota

Submission date
26/03/2019

Recruitment status
No longer recruiting

Registration date
08/04/2019

Overall study status
Completed

Last Edited
12/06/2023

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Patients with cirrhosis (scarring) of the liver are prone to infection. Bacteria which are normally present and confined to the bowel in health can get into the bloodstream in patients with cirrhosis and cause serious and often life-threatening infection with devastating effects on liver function. This is thought to be due to an imbalance in helpful and harmful bacteria in the bowel and problems with the body's immune defence system. Researchers have shown that probiotics, which are 'bio-friendly' food supplements, can alter gut flora and have a number of beneficial effects in cirrhosis. These include an improvement in markers of liver damage and restored function of important immune cells in patients with alcoholic liver disease. They have also been shown to improve outcome and reduce the risk of death in clinical conditions which have a similar basis to chronic liver disease. Probiotics could be very beneficial not only for in-patients who are acutely unwell, but also for out-patients to limit the likelihood of deterioration. This study is designed to assess the effects of a longer treatment with the probiotic Lactobacillus casei Shirota on infection rates, immune function, gut function and quality of life improvement in patients with any form of cirrhosis.

Who can participate?
Patients aged 18-78 with cirrhosis

What does the study involve?
Participants are randomly allocated into two groups. Group 1 receive Yakult yoghurt 3 bottles a day (65 ml each, containing Lactobacillus casei Shirota). Group 2 receive a similar looking and tasting placebo without bacteria. Participants are treated for 6 months. Blood samples are taken at the initial screening visit and at days 0, 14, months 1, 3, 6, 9, and 12. Routine tests are performed. Additional blood samples are collected at day 0, months 1, 6 and 12.

What are the possible benefits and risks of participating?
Previous studies suggest that patients with liver disease do benefit from probiotic therapy in aspects of liver and immune function. Longer treatment with probiotics could reduce significant infection, improve immune function and quality of life. This study is being undertaken if there is

any benefit. Probiotic treatment is a food supplement which is associated with very few risks. We would however avoid using it in patients with inflammation of the pancreas. The main side effects of the supplement are a mild laxative effect and an increase in flatulence, the latter being regarded as a positive indicator of a high degree of fermentation, a sign that the supplements are working.

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
August 2010 to February 2017

Who is funding the study?
Yakult

Who is the main contact?
Prof. Rajiv Jalan
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers
02/0012

Study information

Scientific Title
Prevention of infection in cirrhosis with Lactobacillus casei Shirota: a randomised double-blinded placebo-controlled study

Study objectives
Administration of Lactobacillus casei Shirota in patients with liver cirrhosis will improve innate immune function through alteration of the gut bacterial flora and gut barrier integrity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved by the Joint UCL/UCLH Committees on the Ethics of Human Research: Committee Alpha
Neil Hubbard, Research Portfolio Manager, Theme 4 (NIHR Divisions 6), Royal Free London NHS Foundation Trust, Royal Free Hospital, Research & Development Office, Lower Ground Floor, Room LG/306, Pond Street, London, NW3 2QG; Tel: +44 (0)20 7794 0500 ext: 36316; Email: n.hubbard@nhs.net), REC Ref: 02/0012
Ethics Committee at Basildon Hospital (James Hampton-Till, Director of Research, Basildon & Thurrock University Hospitals NHS Foundation Trust, Nether Mayne, Basildon, Essex, SS16 5NL; Tel: +44 (0)8451553111 ext 8988)

Study design
Multi-centre double-blind placebo-controlled randomised controlled study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format

Health condition(s) or problem(s) studied
Cirrhosis

Interventions
92 patients will be randomised into two groups:
Group 1: Oral Yakult yoghurt 3 bottles a day (65 ml each, containing Lactobacillus casei Shirota at a concentration of 108/ml)
Group 2: Similar looking and tasting oral placebo without bacteria (3 bottles per day)

The recruited patients will be treated for 6 months. Blood will be taken at the initial screening visit and at days 0, 14, months 1, 3, 6, 9, 12. Routine biochemistry and haematology will be performed. Additional blood will be collected at day 0, months 1, 6 and 12. Effect of serum on the function of normal neutrophils will be determined cytokine concentrations, measures of bacterial translocation and intestinal permeability.
Urine collected will be used for further metabolic profiling.

Intervention Type
Supplement

Primary outcome measure
1. Neutrophil function assessed using phagoburst and phagotest at day 0, months 1, 6 and 12
2. Incidence of significant infection documented at time of clinical assessments at day 0, day 14, months 1, 3, 6, 9, 12

Secondary outcome measures
1. Gut barrier function assessed using lactulose/rhamnose/xylose intestinal permeability assay at day 0, months 1, 6
2. Inflammatory, cellular and humoral response assessed using luminex at day 0, months 1,6,12
3. Quality of life assessed using SF-36 at days 0, 14, months 1, 3, 6, 9, 12

Overall study start date
12/08/2010

Completion date
02/02/2017

Eligibility

Key inclusion criteria
1. Patients aged between 18-78 years
2. Clinical and radiological evidence of cirrhosis, and/or biopsy proven liver cirrhosis of any cause
3. Informed consent
4. Abstinence from alcohol for > 2 weeks at the time of screening for inclusion

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
78 Years

Sex
Both

Target number of participants
92

Total final enrolment
92

Key exclusion criteria
1. Pugh score > 10
2. Clinical evidence of active infection
3. Antibiotic treatment within 7 days prior to enrolment
4. Gastrointestinal haemorrhage within previous 2 weeks
5. Use of immunomodulating agents within previous month (steroids etc)
6. Use of proton pump inhibitors for preceding two weeks
7. Concomitant use of supplements (pre-, pro-, or synbiotics) likely to influence the study
8. Renal failure (such as hepatorenal syndrome), creatinine >150 mmol/l
9. Hepatic encephalopathy II to IV
10. Pancreatitis
11. Other organ failure
12. Hepatic or extra-hepatic malignancy
13. Pregnancy

Date of first enrolment
03/05/2011

Date of final enrolment
03/04/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Free Hospital
Pond Street
Hampstead
London
United Kingdom
NW3 2QG

Study participating centre
Basildon and Thurrock University Hospitals NHS Foundation Trust
Nethermayne
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Sponsor information

Organisation
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Sponsor type
University/education

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Industry

Funder Name
Yakult

Results and Publications

Publication and dissemination plan
Planned publication in peer-reviewed journal in 2019.

Intention to publish date
31/12/2019

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		02/06/2020	12/06/2023	Yes	No