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VSL#3 on cardiovascular risk and liver injury in non-alcoholic fatty liver disease

Submission date	Recruitment status	[_] Prospectively registered
08/08/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
09/08/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
28/10/2022	Other	

Plain English summary of protocol

Background and study aims
People with non-alcoholic fatty liver disease (NAFLD) and diabetes are more at risk of developing circulatory problems (cardiovascular disease) such as heart attacks and strokes. It has been suggested that excess bacteria living in the small bowel play a part in causing circulatory problems in these individuals. Toxins produced by bacteria in the small bowel enter the bloodstream where they are transported to the liver, resulting in fat deposition in the liver, liver and blood vessel damage, and a reduction in the bodys responsiveness to insulin. These harmful effects lead to narrowing of blood vessels and the development of circulatory problems. Probiotics are food supplements containing harmless live bacteria which restore gut health. They may potentially lower blood sugar and cholesterol levels, lower blood pressure, improve the body's responsiveness to insulin and reduce inflammation. As such, probiotics may have an added benefit beyond existing treatments to reduce the risk of developing circulatory problems and lessen liver injury.
In our study, we plan to look at whether taking the VSL#3® probiotic supplement will reduce the risk of developing circulatory problems and decrease fat deposition and liver damage. We will also look for potential chemicals in the body that can help us identify people with NAFLD who are at greater risk of getting circulatory problems and are more likely to develop liver damage.

Who can participate?
We aim to recruit 60-70 individuals (both men and women) with non-alcoholic fatty liver disease and type 2 diabetes, age 18 to 70, from diabetes and liver clinics at Queen Alexandra Hospital, Portsmouth.

What does the study involve?
A heart tracing (electrocardiogram) will be done before the study to exclude heart disease. You will attend two visits, 10 weeks apart. Each visit lasts approximately 4 hours. At your first visit, a medical history will be obtained and a physical examination performed. A number of tests will be conducted at each visit. These include blood, urine and stool sampling, a breath test and a liver ultrasound scan. After the first visit, you will be randomly assigned to take either VSL#3® probiotics or a dummy supplement for 10 weeks, and return for your final visit.

What are the possible benefits and risks of participating?
There will be no immediate benefit to those taking part in the study. However, the results may be helpful in the future care of people with NAFLD and type 2 diabetes. A needle will be inserted in your arm to take blood which may leave a small area of bruising after the procedure. You may experience side effects from the medications used in some of the tests carried out. Glyceryl trinitrate may cause headache and flushing. Salbutamol may leave a metallic taste in your mouth. Lactulose may cause bloating, excessive wind and tummy discomfort. These effects are temporary. The study treatment is a food supplement which is considered safe. Bloating may occur initially and is usually short-lived.

Where is the study run from?
Diabetes Centre, Queen Alexandra Hospital, Portsmouth (UK)

When is study starting and how long is it expected to run for?
May 2012 to March 2014

Who is funding the study?
Funding has been provided by Queen Alexandra Hospital, Portsmouth. The study treatment and the dummy product are provided by VSL Pharmaceuticals Inc., Italy.

Who is the main contact?
1. Dr Lina (Pui Lin) Chong (lina.chong@porthosp.nhs.uk)
2. Prof. Michael Cummings (michael.cummings@porthosp.nhs.uk)

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
12470

Study information

Scientific Title

The impact of VSL#3 probiotic on cardiovascular risk and liver injury in patients with non alcoholic fatty liver disease: a randomised, double blinded, placebo controlled proof-of-concept trial

Study objectives
Non-alcoholic fatty liver disease (NAFLD) is strongly linked with tyep 2 diabetes. Existing studies suggest an increased risk of cardiovascular disease in patients with NAFLD independent of features of the metabolic syndrome. There is a graded relationship between the severity of liver disease and cardiovascular risk. It has been proposed that gut microbiota play a vital role in the development and progression of NAFLD. There is a higher prevalence of small intestinal bacteria overgrowth (SIBO) in patients with NAFLD. Delivery of gut-derived endotoxins to the liver triggers a cascade of inflammatory response and insulin resistance implicated in the pathogenesis of NAFLD. At present, there is no cure for NAFLD. Probiotics are non-pathogenic live bacteria which restore gut health and may be beneficial beyond available treatments to lower cardiovascular risk and improve liver injury.

The study aims to test the hypothesis that VSL#3 probiotic supplementation improves biomarkers of cardiovascular risk and liver fat/inflammation in individuals with NAFLD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central - Southampton, 24/01/2012, ref: 11/SC/0532

Primary study design
Interventional

Study design
Randomised interventional trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diabetes Research Network, Oral and Gastrointestinal

Interventions
Two study visits per participant, randomised to receive either treatment or placebo on a 1:1 ratio. Treatment arm will take VSL#3 probiotic 2 sachets twice a day for 10 weeks. Placebo arm will take placebo 2 sachets twice a day for 10 weeks. Participants will stir contents of sachets into cold, non fizzy water and consume orally. Both study arms will be followed up for the same duration i.e. 10 weeks (before and after 10 week course of study treatment).

Intervention Type
Supplement

Primary outcome(s)
Cardiovascular biomarkers pre and post intervention

Key secondary outcome(s)
Liver fat and inflammation - compare fibrosis risk score and structural liver changes before and after study intervention

Completion date
21/03/2014

Eligibility

Key inclusion criteria
1. Individuals with non-alcoholic hepatic steatosis and/or non-alcoholic steatohepatitis (either biopsy proven or based on imaging and exclusion of other causes of liver disease) at high cardiovascular risk (at least 20% risk of a cardiovascular event over the next 10 years)
2. HbA1c less than 10%
3. Age 18 to 70 years
4. Male and female participants

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
35

Key exclusion criteria
1. Individuals with decompensated liver cirrhosis as defined by presence of hepatic encephalopathy, ascites, variceal bleeding
2. Allergy or intolerance to VSL#3 probiotic
3. Insulin treatment
4. Chronic excess alcohol intake (>21units per week for men and >14units per week for women in the last 2 years)
5. Antibiotic treatment 4 weeks prior to the study and/or more than 3 courses of antibiotic treatment over the preceding 6 months
7. Established cardiovascular disease (ischaemic heart disease, cerebrovascular disease and peripheral vascular disease)
8. Individuals with solid organ or bone marrow transplantation
9. Steroid therapy

Date of first enrolment

23/05/2012

Date of final enrolment
21/03/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queen Alexandra Hospital
Portsmouth
United Kingdom
PO6 3LY

Sponsor information

Organisation
Portsmouth Hospitals NHS Trust (UK)

ROR
https://ror.org/009fk3b63

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Portsmouth Hospitals NHS Trust (UK)

Funder Name
VSL Pharmaceuticals, Inc (Italy)

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/04/2021	28/10/2022	Yes	No