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Does treatment with bile acid tablets improve blood sugar levels and assist in weight loss

Submission date
25/08/2023

Recruitment status
No longer recruiting

Registration date
11/09/2023

Overall study status
Completed

Last Edited
05/02/2026

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Bile salts are natural substances made in the liver which help to digest food. They are also involved in the regulation of gut hormones, which are secreted in response to food. Gut hormones are important because increasing their levels has been shown to help improve diabetes and reduce weight. Ursodeoxycholic acid (UDCA) and chenodeoxycholic acid (CDCA) are both types of bile acids that can be given in tablet form. They have been commonly used for many years as a treatment for gallstones – and have few side effects. This study will investigate whether a six-week course of UDCA or CDCA increases gut hormone secretion in diabetic patients. It will test our theory that increased levels of bile acids in the circulation will increase gut hormone release, improve weight and improve insulin sensitivity (how sensitive your body is to the hormone insulin). It may help us develop new treatments for patients with diabetes or those who are overweight.

Who can participate?
Anyone aged between 18-80 years old who is prediabetic or has confirmed type 2 diabetes, on no ant-diabetic medication or only ONE medication

What does the study involve?
Patients will attend an initial screening visit which will confirm their eligibility to take part in the study. This will involve a brief medical questionnaire and examination, blood tests, a urine test, heart tracing and measurements of their blood pressure, and heart rate. Patients who take any anti-diabetic medication will be asked to withhold this for the duration of the study and be closely monitored by the research team.

There are then four visits with two of those being overnight stays.
Visit 1 and 3: (at 0 and 6 weeks). These visits will require an overnight stay. Patients will be asked to come into the clinical research facility fasted and to have taken all their study tablets one hour before the start of the test. They will then have the mixed meal test (MMT). This involves drinking a nutritional milkshake and having a cannula inserted (a flexible tube with a needle at one end) into a vein in one of their arms. From this cannula, several blood samples will be taken over the next three hours.

Following the end of the MMT, they will be offered a standardised meal for lunch and dinner and then remain overnight at the clinical research facility where they will fast from 10 pm. They may need to be started on an insulin infusion to keep their blood glucose stable. During the next day, how sensitive their body is to insulin will be measured with a glucose clamp. To do so, a glucose tracer, together with insulin and dextrose will be given through the first cannula whilst blood will be taken from the other one for testing. This tracer will not cause any negative effects. Blood will be taken multiple times during the study for analysis and the test can take up to 7-8 hours to complete. At the end of the study, patients will be given something to eat and drink and then be discharged once the team are happy that their blood sugars are stable.

Visit 2 and 4: (at 3 and 8 weeks). On these visits, they will undergo the MMT without the glucose clamp study. After the visit 3 (6 weeks), they will be asked to stop treatment. During every visit, they will undergo measurements to check their height, weight, vital signs (heart rate and blood pressure) and a urine test. Resting energy expenditure (the amount of calories you burn) will also be determined using a machine that measures the amount of oxygen and carbon dioxide they are breathing. They will also be asked to provide a stool sample for all four visits and will given a simple kit so you can collect this at home. This is to look for any signs of fat malabsorption and study the gut bacteria.

What are the possible benefits and risks of participating?
Benefits from the study will include an in-depth assessment and monitoring of the patient's blood glucose levels, information regarding their general health including metabolism, body composition and response to insulin and an opportunity to discuss with the research team regarding any aspect of their care. They may or may not experience some improvement in blood sugar levels whilst on the trial and may or may not lose weight.

The most common side effect of taking part includes discomfort and bruising at the cannulae insertion sites. Very rarely blood sugar levels can become low during the clamp test; this will be promptly treated by the research team if it happens. Withholding diabetic medication with well-controlled diabetes carries a small risk that blood sugar levels may increase to a dangerous level. This is unlikely to occur in patients whose diabetes is only diet controlled or who are only on one anti-diabetic medication and who will be off medication for only 8 weeks. Blood glucose will be closely monitored throughout this period. Bile acids such as those being administered in the study are currently licensed for use for various conditions in the UK. The study will be using the same dose and whilst they have some side effects such as abdominal cramps, bloating or diarrhoea, these are thankfully quite rare.

Where is the study run from?
Hammersmith Hospital (UK)

When is the study starting and how long is it expected to run for
October 2020 to July 2025

Who is funding the study?
1. Novo Nordisk UK Research Foundation (UK)
2. Leadiant Bioscience (Supplied the bile acids) (Italy)

Who is the main contact
Dr Yasmin Tabbakh (Clinical Research Fellow), ytabbakh@imperial.ac.uk (UK)

Contact information

Type(s)
Public

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Additional identifiers

Integrated Research Application System (IRAS)
292604

Central Portfolio Management System (CPMS)
48464

Study information

Scientific Title
Bile acid remediation of diabetes and obesity study

Acronym
BARDOS

Study objectives
1. Bile acids chenodeoxycholic acid (CDCA) and ursodeoxycholic acid (UDCA) are able to stimulate the secretion of enteroendocrine L-cell gut hormones such as Glucagon-like peptide -1 (GLP-1), oxyntomodulin (OXM) and peptide YY (PYY)
2. UDCA is capable of improving insulin sensitivity
3. CDCA is capable of increasing resting energy expenditure

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 12/04/2021, HRA and Health and Care Research Wales (HCRW) Approval (Castlebridge, 5 - 19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0) 2920230457; approvals@hra.nhs.uk), ref: 21/WM/0054

Primary study design
Interventional

Study design
Double-blind randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Prediabetes and type 2 diabetes

Interventions
It is known that following weight loss surgery such as roux en y gastric bypass, there is an increase in the delivery of bile acids to the small intestine, with subsequent weight loss /improvement in blood glucose control. Overall there are higher levels of bile acids within the bloodstream in post-operative patients. The main hypothesis of this study is whether treatment with bile acid medication in patients who are type 2 diabetic and have a raised BMI will result in improvements in those parameters thus emulating the effects of bariatric surgery.

There are three arms in the study in total. In two intervention arms, treatment may be with either a primary bile acid (chenodeoxycholic acid) or a secondary bile acid (ursodeoxycholic acid), and there is a placebo treatment, which in this case it is Boots brand low-dose Vitamin C tablet 500mg. Participants are randomised by an unblinded member of the team using randomisation by minimisation method and will be stratified according to HbA1c.

Treatment is given over a six-week period orally and the dosage of treatment is calculated dependent on a participant's body weight and utilises current BNF dosage. Chenodexocycholic acid is dosed at 13-16mg/kg with a maximum dose of 1000mg a day. Ursodeoxycholic acid is dosed at 12-16mg/kg a day with a maximum of 1750mg a day. The amount is given in divided doses (twice a day). The placebo tablet (vitamin C) is given as one tablet twice a day to maintain consistency. Follow-up and monitoring of side effects will be undertaken at each study visit with clinical history/examination and blood test monitoring.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Chenodeoxycholic acid, ursodeoxycholic acid

Primary outcome(s)
Gut hormone secretion measured using venepuncture following a standardised mixed meal tolerance (MMT) test at -60, 0, 15, 30, 60, 90, 120 and 240 minutes

Key secondary outcome(s)
1. Bodyweight change measured using the TANITA body composition scales at each stud visit (visit 1 at 0 weeks, visit 2 at 3 weeks, visit 3 at 6 weeks and visit 4 at 8 weeks)
2. Insulin sensitivity (hepatic and peripheral) measured using the two-step euglycaemic hyperinsulinaemic clamp method. 6, 62H2 glucose isotope will be infused prior to the clamp until a state of equilibrium is reached then the first step of the clamp (hepatic phase) is commenced which lasts 2 hours. The second step is the peripheral phase which also lasts 2 hours. Blood glucose measurements will be taken at 10-minute intervals using a YSI glucose/lactate analyzer alongside samples for glucose and insulin at -120, 0, 30, 60, 90, 100, 110, 120, 150, 180, 210, 220, 230 and 240 minutes.
3. Energy expenditure measured using indirect calorimetry before and after the mixed meal tolerance (MMT) test

Completion date
31/07/2025

Eligibility

Key inclusion criteria
1. Aged between 18-80 years old
2. BMI ≥22 kg/m2
3. Diagnosed with type two diabetes mellitus (T2DM) according to WHO 2006 10 and WHO 201111 criteria ≥6 months but less than 10 years
4. HbA1c ≥42 mmol/mol and ≤75 mmol/mol
5. If there are concerns about the stability of glycaemic control then two measurements of HbA1c varying by no more than ±11 mmol/mol on two measurements separated by at least 30 days will be done. If no concerns regarding stability then this does not need to be done
6. T2DM treated with either lifestyle measures, monotherapy with metformin, sulphonylurea, sodium-glucose co-transporter-2 (SGLT-2) inhibitor, or dipeptidyl
peptidase-4 (DPP-IV) inhibitor
7. Liver function tests up to 1.5x the upper limit of normal

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
80 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Unable to give informed consent
2. Hepatobiliary, gastrointestinal or other diseases which in the opinion of the study investigators will compromise participant safety or the scientific value of data obtained
3. Functional diarrhoea with stool frequency ≥5 times a day
4. Current treatment with GLP-1 analogues or insulin
5. Sensitivity to CDCA or UDCA in the past
6. Current pregnancy (women with childbearing potential will be asked to use high-reliability methods of contraception during the study)
7. Alcohol in excess of NHS recommended weekly allowance or substance misuse
8. Previous gut resection which in the opinion of the PI will affect the results of the study

Date of first enrolment

01/08/2021

Date of final enrolment
30/04/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Hammersmith Hospital
Clinical Research Facility
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Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Industry

Funder Name
Novo Nordisk UK Research Foundation

Alternative Name(s)
Novo Nordisk UK Research Foundation (NNUKRF), The Novo Nordisk UK Research Foundation, ovo Nordisk Research Foundation UK, NNUKRF

Funding Body Type

Private sector organisation

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

Location
United Kingdom

Funder Name
Leadiant Biosciences

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Yasmin Tabbakh, ytabbakh@imperial.ac.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article			05/02/2026	Yes	No
Protocol file	version 2.2	29/06/2021	10/01/2024	No	No