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Effect of Metformin on gut microbiota and pancreatic beta cells function in patients with type 2 diabetes

Submission date
19/07/2015

Recruitment status
No longer recruiting

Registration date
09/09/2015

Overall study status
Completed

Last Edited
08/09/2015

Condition category
Nutritional, Metabolic, Endocrine

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Gut microbiota is the term used to refer to the bacteria that naturally live in our intestines. It has an effect on numerous biological functions. Recent research suggests that its composition (i.e. what type of bacteria is making up the microbiota) may contribute to the development of metabolic disorders, such as diabetes, by affecting the physiology and metabolism of an individual. Metformin is one of the most widely prescribed type 2 diabetes (T2DM) treatments. Metformin-induced changes in the gut microbiota have been reported; however, the relationship between metformin treatment and the gut microbiota remains unclear. This study investigates whether the anti-diabetic effect of metformin is related to changes in the composition of gut microbiota.

Who can participate?
Adults aged between 18-79 with T2DM, treated with two or more oral anti-diabetic drugs for at least 3 months and a BMI≥18.5kg/m2

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given insulin plus metformin. Those in group 2 are given insulin only. The study takes place over a 16 week period during which time changes in gut microbiota are measured once a month.

What are the possible benefits and risks of participating?
The metformin treatment may be related to alterations of intestinal microbial composition and improve a participants T2DM directly or indirectly. There is a risk that the treatment may be of no benefit.

Where is the study run from?
Qilu Hospital ,Shandong University (China)

When is the study starting and how long is it expected to run for?
June 2015 to January 2016

Who is funding the study?
Qilu Hospital, Shandong University (China)

Who is the main contact?
Mr Anju Zuo

Contact information

Type(s)
Scientific

Contact name
Mr Anju Zuo

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Additional identifiers

Protocol serial number
2015041

Study information

Scientific Title
A prospective, randomized, open-label, parallel controlled, single-center trial, examining the effect of Metformin on gut microbiota and pancreatic beta cells function in patients with type 2 diabetes

Study objectives
1. The gut microbiota and their metabolic pathways will be influenced by Metformin treatment in patients with type 2 diabetes
2. Metformin maybe ameliorate islet function by improving dysbiosis of gut micobiota in patients with type 2 diabetes

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical Committee of drug clinical trials, Qilu Hospital, Shandong University, 25/05/2015, ref: 2015041

Study design
Prospective, randomized, open-label, parallel controlled, single-center trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 2 diabetes (T2DM) patients with oral anti-diabetic drugs (OAD) losing efficacy

Interventions
1. 30 patients with OAD losing efficacy receiving insulin plus metformin
2. 30 patients with OAD losing efficacy receiving insulin monotherapy

Intervention was for 16 weeks.

Intervention Type

Primary outcome(s)
Identifying the change of composition of gut microbiota by 16s rRNA technology

Measured once a month over the study period.

Key secondary outcome(s))
1. Achievement of HbA1c
2. Achievement of weight loss
3. Change in HbA1c
4. Waist circumference
5. Fasting blood glucose
6. Lipids and CRP
7. LPSIL-6mRNAIL-1BmRNACD4/CD8 and Foxp3Tre

They will be measured once a month.

Completion date
25/01/2016

Eligibility

Key inclusion criteria
1. Diagnosed with T2DM
2. Treated with two or more OADs for more than three months with blood glucose HbA1c≥7% within 14 days of the screening day
3. Aged between 18 to 79
4. BMI≥18.5kg/m2
5. According to investigators' judgment, subjects are able and willing to obey the following instructions:
5.1. During the whole study, treatment will be continued according to the requirements in the protocol
5.2. During the whole study, diet will be maintained according to the requirements in the protocol

5.3. Participation in regular visits, and willing to receive telephone follow-up
5.4. Women that are able to conceive (and men whose partner can conceive) are willing to be given contraceptive treatment during the whole study
6. Participants must be male, or non-pregnant females who are not breastfeeding
7. Participants must be without metformin contraindications
8. All participants must sign informed consent form before any study relevant activities have been conducted

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Participants diagnosed with type 1 diabetes
2. Previously treated with insulin for more than 14 days continuously within 3 months before screening visit or within one month before the patient entering the study
3. Diagnosed with any of the following cardiovascular diseases within three months before screening visit: acute myocardial infarction, heart function classification III/IV according to New York Heart
Association, congestive heart failure with left ventricular ejection fraction ≤ 40%, or cerebrovascular events (apoplexy)
4. Impaired liver function, with obvious clinical signs or symptoms of liver disease, acute or chronic hepatitis, or ALT/AST levels ≥2.0 times of the upper limit of the reference range at the screening visit
5. Serum creatinine ≥1.5mg/dl (133 μmol/L) for men, ≥1.4mg/dl (124 μmol/L) for womenor eGFR<45ml/min/1.73m2
6. Known to have proliferative retinopathy or maculopathy which needs an urgent treatment by the investigator’s judgment
7. Repeated severe hypoglycemia and hypoglycemia consciousness disorders by investigators’ judgment
8. Persistent uncontrolled hypertension (systolic blood pressure ≥180mmHg, or diastolic blood pressure ≥105mmHg)
9. Severe chronic gastrointestinal diseases
10. History of diabetic ketoacidosis or hypertonia condition/coma once or more than once;
11. Receiving long-term (>14 days) systemic glucocorticoid treatment (external use, intraocular, inhaled or intranasal preparations except) or received this type of treatment within four weeks before screening visit; During the whole study, any treatment which can affect glucose regulation should be avoided, as thyroid medication, estrogen, oral contraceptives, phenytoin, niacin, sympathomimetic drugs and isoniazid
12. Hematological system diseases which maybe affect HbA1c value (as hemolytic anemia, sickle

cell disease)
13. Any conditions which may affect patients follow and complete the study protocol (as known drug abuse, alcoholic, mental diseases)
14. Currently in a study or 30 days before recruiting withdrawing from a study which involves the investigational medicinal product or not approved drugs or instruments; or participating other types of clinical studies at the same time and not suitable to participate in this study judged by investigators from medical or science perspectives
15. Allergic to metformin/insulin or with metformin/insulin contraindication
16. Combined with severe lung diseases or history of hypoxia
17. Combined with endocrine diseases as hypercortisolism; patients with thyroid diseases under control of drugs for more than half year can be included;
18. Stress state as surgery, acute craniocerebral injury etc
19. Vitamin B12 deficiency without correction

Date of first enrolment
25/07/2015

Date of final enrolment
30/01/2016

Locations

Countries of recruitment
China

Study participating centre
Qilu Hospital, Shandong University
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250012

Sponsor information

Organisation
Qilu Hospital, Shandong University

ROR
https://ror.org/056ef9489

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Qilu Hospital, Shandong University

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Other