Effect antibiotics on gutmicrobiota composition & insulin resistance.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24894

Source
NTR

Brief title
A-V trial

Health condition

insulin resistance, obesity

Sponsors and support

Primary sponsor: Academic Medical Center, Amsterdam
Source(s) of monetary or material Support: iniator=sponsor (self-financing research)

Intervention

Outcome measures

Primary outcome

The primary endpoint is changes in faecal flora composition after 7 days as well as 2, 4 and 6 weeks after the antibiotics.

Secondary outcome

1. Changes in insulin resistance (assessed by hyperinsulinemic normoglycemic clamp at baseline and after 7 days);

2. Bile acid and lipidmetabolism (assessed by MMT at baseline and after 7 days);

3. Changes in systemic inflammatory markers and lipid profiles at baseline as well as 7 days, 2, 4 and 6 weeks after antibiotics.

Study description

Background summary

Objective:

To investigate the effect of antibiotic intervention on gut microbiota composition, insulin resistance and bile acid composition.

Study design:

Two-arm, randomised, controlled single centre trial.

Study Population:

Male obese subjects with metabolic syndrome (BMI > 30kg/m2, FPG>5.6 mmol/l), age 20-65 yr, no medication use.

Treatment:

Patients will be randomised to either 7 days amoxicillin 500mg 3dd or 7 days vancomycin 250 mg 3dd 2.

Outcome measures:

The primary endpoint is changes in faecal flora composition after 7 days as well as 2, 4 and 6 weeks after the antibiotics. Secondary endpoints are changes in insulin resistance (assessed by hyperinsulinemic normoglycemic clamp at baseline and after 7 days), bile acid and

lipidmetabolism (assessed by mixed meal test at baseline and after 7 days), as well as changes in systemic inflammatory markers and lipid profiles at baseline as well as 7 days, 2, 4 and 6 weeks after antibiotics.

Sample Size:

It is estimated that a total of 10 patients in each arm are needed.

Study objective

Accumulating data from both patients and animal models indicates that imbalances in the composition of the gut microbiota are related to obesity and its associated diseases However, the exact role of the microbiota and the mechanism mediating its impact on metabolic functions are poorly understood.

Interestingly, antibiotics have been shown to produce drastic short- and long-term alterations of the human indwelling microbiota. After a 2 wk intervention with norfloxacin in combination with ampicillin the numbers of aerobic and anaerobic gut bacteria in ob/ob mice were maximally suppressed. The ob/ob mice showed a significant improvement in fasting glycemia and oral glucose tolerance by 30%. Concomitant reduction of liver triglycerides, reduction of lipopolysaccharides supported the antidiabetic effects of antibiotic treatment. This study showed that modulation of gut microbiota with antibiotics improved glucose tolerance in mice by altering the expression of hepatic and intestinal genes involved in inflammation and metabolism.

The mechanism by with gutmicrobiota affect glucose metabolism remains elusive, however some studies have suggested that bileacids are involved in human glucose and lipid metabolism We postulate that insulin resistance can be reduced reducing the numbers of specific gut microbiota by certain antibiotics. To test this hypothesis, we would like to investigate the effect of antibiotic treatment on gut microbiota composition, insulin resistance and bile acid metabolism in obese subjects.

Study design

Baseline and 1,2,4 & 6 weeks after antibiotics.

Intervention

Patients will be randomised to either 7 days amoxicillin 500mg 3dd or 7 days vancomycin 500mg 3dd.

Contacts

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Eligibility criteria

Inclusion criteria

1. Male obese subjects with metabolic syndrome (BMI > 30kg/m2, FPG>5.6 mmol/l);

2. Age 20-65 yr;

3. No medication use.

Exclusion criteria

1. Patients with renal failure (kreatinine>135mmol/l);

2. Liver function problems (ASAT/ALAT>2x upper limit);

3. Hypersensitivity to penicillin, amoxicillin, other beta lactams or chinolones;

4. Patients with medication known to interfere with glucose metabolism or bile acid composition (sequestrants, chenodiole, ursochol);

5. Patients with infectious mononucleosis;

6. Asthmatic patients;

7. Antibiotic use last three months;

8. Disorders known to interfere with bile acid metabolism (intestine resection, liver/intestine disorders);

9. History of laparoscopic cholecystectomy;

10. Patients with idiopathic diarrhea.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2011
Enrollment:	20
Type:	Anticipated

Ethics review

Positive opinion

Date:	15-10-2010
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL2448
NTR-old	NTR2566
Other	MEC AMC : 10/265
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A