

Effect antibiotics on gutmicrobiota composition & insulin resistance.

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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...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24894

Bron

NTR

Verkorte titel

A-V trial

Aandoening

insulin resistance, obesity

Ondersteuning

Primaire sponsor: Academic Medical Center, Amsterdam

Overige ondersteuning: initiator=sponsor (self-financing research)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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 which gut microbiota affect glucose metabolism remains elusive, however some studies have suggested that bile acids are involved in human glucose and lipid metabolism. We postulate that insulin resistance can be reduced by 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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Male obese subjects with metabolic syndrome ($BMI > 30\text{kg/m}^2$, $FPG > 5.6\text{ mmol/l}$);
2. Age 20-65 yr;
3. No medication use.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Patients with renal failure ($\text{kreatinine} > 135\text{mmol/l}$);
2. Liver function problems ($\text{ASAT/ALAT} > 2\times$ 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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blinding:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland	
Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-01-2011
Aantal proefpersonen:	20
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies	
Datum:	15-10-2010
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten

N/A