Effect of resveratrol on insulin sensitivity and metabolic profile in type 2 diabetics

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON37515

Source
ToetsingOnline

Brief title
Resveratrol and type 2 diabetes

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Lipid metabolism disorders

Synonym
obesitas and sugar

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: metabolism, mitochondrial function, Resveratrol, type 2 diabetes

Outcome measures

Primary outcome

The main study endpoints are the differences in whole body- and muscle insulin sensitivity, and mitochondrial fat oxidative capacity after 30 days of resveratrol supplementation compared to the placebo trial.

Secondary outcome

Secondary outcome measures are the changes in liver and muscle fat storage after 30 days of resveratrol or placebo supplementation.

Study description

Background summary

There is now a general consensus that the combination of excessive energy intake and a low capacity to oxidize fat will lead to muscular fat accumulation and insulin resistance. It is known for many years that physical activity and diet therapy are the most powerful treatment to combat obesity and insulin resistance, but it is also known that it is difficult to get people to exercise and follow diets. A major breakthrough in this field has come from the nutrition field, with the finding that resveratrol, a natural polyphenolic compound, could serve as an *calory restriction mimetic*, as a recent study of S. Timmers et al. in Cell metabolims (2011) showed that resveratrol mimiced the effect of caloric restriction in healthy obese man (lowering liver fat accumulation and increasing fat oxidation, thereby improving metabolic health in these subjects). These findings were similar to those found earlier in animal studies, where it was found that resveratrol protected mice from many detrimental effects of diet-induced obesity. Therefore we would like to investigate if resveratrol has the same effects in obese humans with type 2 diabetes as it does in healthy obese man.
This information can then be used to develop new treatment for obesity and type 2 diabetes. Therefore, we would like to investigate whether ResvidaTM can increase mitochondrial number together with an increased intrinsic activity and whether this will lead to a better insulin sensitivity in type 2 diabetic

patients.

Study objective

To examine whether resveratrol supplementation in type 2 diabetic patients improves overall and muscle-specific insulin sensitivity by affecting mitochondrial fat oxidative capacity. Furthermore, we are interested is this also affects liver and muscle fat storage.

Study design

24 obese (BMI 27-35 kg/m2) male subjects with type 2 diabetes, aged between 40 and 70 years, who are not engaged in regular programmed exercise are included in a randomized, double blind cross over design. Each subject will participate in two interventions, in random order, and separated by a wash-out period of at least 4 weeks. Each intervention includes a 30 days (4 week) suppelementation with resveratrol or placebo. Before the start of the study, subjects will be screened to assess elegibility., which will include a medical questionnaire, a measurement of body weight and composition (DEXA scan) to determine fat content, and drawing of a fasted blood sample. On day 0, subjects will come to the university for withdrawal of a fasted blood sample and a measurement of body weight. Hereafter, heart rate and blood pressure will be checked and an ECG will be made by an experienced physician. Thereafter, subjects can go home and they will receive enough capsules for the first week of the intervention. Additional blood samples will be drawn on a weekly basis as well as measurements of body weight (day 7, 14, 21). During these weekly visits, subjects will receive enough capsules for the next week. On day 27, subjects will report to the university for a maximal aerobic capacity test under the supervision of a physician. An ECG will be made during the cycling test. On day 29, hart function will be measured by echocardiography, and in vivo mitochondrial function and liver fat content will be measured with MR spectroscopy. Thereafter, subjects will stay in the respiration chamber for 12 hours (evening day 29 and night day 29) during which their energy expenditure and fat oxidation will be measured. On day 30 in the morning, subjects will leave the respiration chamber, and a fasting blood sample will be drawn. An ECG will be made and blood pressure and heart rate will be measured. Then, fat content in the heart will be measured by MR spectroscopy and a muscle biopsy will be taken. Hereafter, the insulin sensitivity measurement will be started to determine overall and muscle and liver specific insulin sensitivity. After the test, a second muscle biopsy will be taken.

Intervention

Subjects will be asked to take two pills of resveratrol 75 mg, or placebo, twice daily (lunch and diner), for 30 days, which will be randomized. Resveratrol (resvidaTM) is a food supplement and is regulated in the body as a

food component. ResvidaTM and placebo are provided by DSM Nutritional Products Ltd. For the resveratrol product, the maximal approved daily dose in humans is 150 mg/day. For higher doses the safety concerns are not yet investigated. Therefore, we have chosen to supplement the subjects with a dose of 150 mg/day spread out over two doses of 75 mg twice a day with lunch and diner.

Study burden and risks

Before the start of the study, subjects will be screened to access eligibility which will include a medical questionnaire, measurement of body weight and body composition (DEXA scan). A fasted bloodsample will also be drawn (duration: 1 hour). Thereafter, they will be randomized and undergo two intervention periods of 30 days separated by a wash-out period of at least 4 weeks. The subjects will come to the University 6 times (day 0, 7, 14, 21, 27, 29). During these visits at the University, a bloodsample will be taken weekly as well as a weekly measurement of body weight (day 0, 7, 14, 21), a maximal aerobic capacity test will be performed (day 27) and heart function will be measured by echocardiography, in vivo mitochondrial function and liver fat content will be measured with MRS (day 29). In addition, subjects will stay in the respiration chamber for 12 hours (1 evening and night) (day 29-30) after which the fat content of the heart will be measured by MR spectroscopy (day 30), and a muscle biopsy will be taken (day 30). Hereafter, the insulin sensitivity test will be started (day 30). After this test is finished, a second muscle biopsy will be taken (day 30).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Male sex
* Age: 40-70 years
* Body fat percentage >25, BMI 27-35 kg/m2
* Diagnosed with type 2 diabetes at least one year before the start of the study
* Well-controlled type 2 diabetics: HBA1C < 8.0%
* Oral glucose lowering medication (metformin only or in combination with sulfonylurea agents)
* Sedentary (Not more than 2 hours of sports a week, no active job that requires strenuous physical activity)
* Stable dietary habits
* Willingness to abstain from resveratrol-containing food products

Exclusion criteria

* Unstable body weight (weight gain or loss > 3kg in the last three months)
* Total body fat percentage < 25%
* Hemoglobin <7.8 mmol/l
* Engagement in programmed exercise > 2 hours total per week
* Impaired kidney and/or hepatic function
Creatinine 50-100 umol/L;Liver enzymes, within 2 times of normal range of laboratory standard
(ASAT <60 U/L, ALAT <70 U/L, Billi <40 umol/L, gamma-GT <80 U/L)
* No diabetes related co-morbidities like cardiovascular diseases, diabetic foot, polyneuropathy, retinopathy.
* Insulin dependent Diabetic subjects.
* Anti-coagulants
* Insulin therapy
* Intake of dietary supplements except vitamins and minerals
* Unwillingness to restrict high-resveratrol-containing food products
* Current alcohol consumption > 20 grams/day
* Participation in another biomedical study within 1 month before the first screening visit

* Any contraindication to MRI scanning. These contra-indictations include patients with following devices:
o Central nervous system aneurysm clip
o Implanted neural stimulator
o Implanted cardiac pacemaker of defibrillator
o Cochlear implant
o Insulin pump
o Or metal containing corpora aliena in the eye or brains
* Subjects who don*t want to be informed about unexpected medical findings during the screening /study, or do not wish that their physician is informed, cannot participate in the study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-06-2013
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	23-04-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
CCMO	NL39010.068.11