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Zinc supplementation and exercise to improve therapy for type 2 diabetes

Submission date
06/11/2018

Recruitment status
No longer recruiting

Registration date
21/12/2018

Overall study status
Completed

Last Edited
10/10/2022

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
Type 2 diabetes is a widespread disease responsible for long term severe dysfunction of several organs. It involves problems with insulin production and function. Diabetes affects a large proportion of the population worldwide. While there are drugs designed to improve insulin production and action, it is clear that this is not enough to an appropriate management of this pathology.
Zinc is an essential nutrient that participates in insulin secretion in the pancreas, and also is able to help insulin function in muscle and other peripheral tissues. Exercise is also known to have positive effects on diabetes. As it is vital to improve diabetes treatment, it is important to determine if zinc and exercise can work synergistically - if the effects of both treatments together is better than either treatment individually.
This study aims to study the effects and mechanisms of supplementation with zinc and muscle strength training, compared to zinc supplementation alone, muscle strength training alone or standard diabetes control advice on insulin and metabolism in people with type 2 diabetes.

Who can participate?
Adults aged 35-69 with type 2 diabetes who have been diagnosed for less than 15 years

What does the study involve?
All participants will receive the standard treatment for diabetes. In addition, they will be randomly allocated to four groups:
1. Control group: This group will receive a placebo capsule and no muscle strength training
2. Zinc group: This group will receive zinc capsules (40 mg) to take once daily for 24 weeks, and no muscle strength training
3. Muscle strength training group: This group will receive the placebo capsule and a 24 week personalised muscle strength training program
4. Zinc and muscle strength training group: This group will receive zinc capsules (40 mg) to take once daily for 24 weeks and a 24 week personalised muscle strength training program
The muscle strength training will involve 3 sessions per week for 12 weeks and then 1 session per week for the following 12 weeks. Sessions will be personalised and consist of both supervised sessions and at-home sessions

What are the possible benefits and risks of participating?
The participants may benefit from receiving special medical and dietetic attention during the study. Participants will also be monitored by a range of labatory tests, which may help to improve their control of their diabetics. this will help to a better control of the condition.
The possible risks of participating include potential pain or bruising from blood sampling, and metabolic alteration during the intravenous glucose tolerance test.

Where is the study run from?
Department of Nutrition, Faculty of Medicine, University of Chile, Santiago (Chile)

When is the study starting and how long is it expected to run for?
April 2016 to March 2020

Who is funding the study?
National Fund for Development of Science and Technology (FONDECYT) Research project 1160792 (Chile)

Who is the main contact?
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Contact information

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Additional identifiers

Protocol serial number
FONDECYT 1160792

Study information

Scientific Title
The interaction between supplemental zinc and muscle strength training as a key element to improve therapy for type 2 diabetes

Study objectives
Zinc supplementation plus muscle strength training in type 2 diabetic individuals will decrease insulin resistance, and consequently will improve the clinical and metabolic condition of diabetes and enhance glucose-stimulated insulin secretion, when compared with type 2 diabetic subjects treated with zinc alone, or muscle-strength training alone, or those receiving the regular diabetes-control advice alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Comite de etica de investigación en seres humanos. Facultad de Medicina, Universidad de Chile (Ethics Committee for Research in Humans, Faculty of Medicine, University of Chile), 24/05/2016, Project 088-2016

Study design
Interventional double-blinded randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 2 diabetes

Interventions
Participants will be randomly allocated to one of four groups:
1. Control group (C): placebo and no muscle strength training
2. Zinc (Zn): 40 mg per day of zinc and no muscle strength training
3. Muscle strength training (MST): placebo and muscle strength training
4. Zinc plus muscle strength training (ZnMST): 40 mg per day of zinc and muscle strength training
Randomisation will be carried out using random number tables by a medical technologist.
Those allocated to receive zinc will receive one 40 mg capsule per day of zinc for 24 weeks.
Those allocated to receive the muscle strength training program will undergo 12 weeks (3

sessions per week) of individually-supervised and at home strength training using body weight with moderate loads and repetitions. This will be followed by 12 weeks with 1 session per week. All individuals will also receive standard treatment for type 2 diabetes as suggested by the American Diabetes Association.
Participants and investigators will be blinded with regard to zinc supplementation.
The intervention will last for 24 weeks.

Intervention Type
Mixed

Primary outcome(s)
An intravenous glucose tolerance test after an overnight fast will be complete, with blood samples drawn 15 and 5 minutes before a glucose bolus (0.3 g/kg body weight as 50% glucose in saline solution) administered over 2 minutes. Samples will then be drawn at 2, 3, 4, 5, 6, 8, 10, 12, 14, 19, 22, 24, 27, 30, 40, 50, 70, 90, 120, 150, and 180 min after the bolus. Insulin (0.05 U/kg body weight) will be infused over 5 minutes, beginning 20 minutes after the glucose bolus. The data will be analysed using the MINMOD program for the following insulin sensitivity indices:
1. Insulin sensitivity (Si)
2. Acute insulin response to glucose (AINg)
3. Glucose effectiveness (Sg)
4. Fractional metabolic clearance rate of insulin (kI)
5. Disposition index (DI)
This procedure will be carried out at the baseline and after 24 weeks.

Key secondary outcome(s))
1. Clinical control of diabetes, assessed using a blood pressure, skin and comprehensive foot examination carried out by a Diabetes Nutrition specialist physician at the baseline and after 12 and 24 weeks
2. Anthropometric parameters, assessed using standardised methods at the baseline and after 24 weeks:
2.1. Weight, assessed using a measuring scale
2.2. Height, assessed using a stadiometer
2.3. Waist circumference, assessed using a measuring tape
3. Food and nutrient intake, assessed using food history and three-day record questionnaires at the baseline and after 24 weeks
4. Body composition, assessed using dual X-ray absorptometry (DXA) at the baseline and after 24 weeks
5. Zinc status parameters:
5.1. Plasma zinc, assessed using atomic absorption spectrophotometry of blood samples at the baseline and after 12 and 24 weeks
5.2. Size of the rapidly exchangeable zinc pool, assessed using stape isotope methodology from spot urine samples taken from days 3-8 after infusion
6. Metabolic status under overnight fasting conditions, assessed using clinical laboratory routine procedures of blood samples at the baseline and after 12 and 24 weeks:
6.1. Plasma HbA1c levels, assessed using high-performance liquid chromatography
6.2. Glucose levels, assessed using an endpoint colorimetric assay
6.3. Haemoglobin levels, assessed using a Coulter counter
6.4. Lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides), assessed using an endpoint colorimetric assay
7. Plasma inflammation markers, assessed from blood samples at the baseline and after 12 and 24 weeks:

7.1. Plasma high-sensitive C-reactive protein (CRP), assessed using immunoturbidimetry
7.2. Adiponectin, assessed using ELISA
7.3. Tumour necrosis factor alpha (TNFα), assessed using ELISA
7.4. IL-6, assessed using ELISA
8. Oxidative stress markers, assessed at the baseline and after 12 and 24 weeks:
8.1. Plasma F2-isoprostane, assessed using ELISA
8.2. Thiobarbituric acid reactive substances (TBARS), assessed using the Cell Biolab Inc TBARS Assay Kit
8.3. Red blood cell glutathione, assessessed using the Cayman Chemical Glutathione Assay Kit
9. Analysis of zinc-related gene expression (mRNA and sirtuins), assessed using real-time PCR after isolation of peripheral blood mononuclear cells (PBMNC) at the baseline and after 24 weeks
10. Physical activity and fitness, assessed at the baseline and after 12 and 24 weeks:
10.1. Physical activity, assessed using 3 axis accelerometers over a 7 day period
10.2. Muscle mass functionality, assessed using:
10.2.1. 30 second sit-to-stand test
10.2.2. Hand grip strength test

Completion date
31/03/2020

Eligibility

Key inclusion criteria
1. Aged 35-69 years
2. Type 2 diabetes
3. Diagnosed with type 2 diabetes for less than 15 years
4. Sedentary, defined as less than 3 sessions per week of 30 minutes of physical activity and/or sport
5. BMI 20-40 kg/m² for at least 3 months prior to screening
6. Stable body weight (variation <5%) for at least 3 months prior to screening
7. Glycated haemoglobin (HbA1c) 6.5-9.0% and/or fasting glycemia <180 mg/dL

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
104

Key exclusion criteria
1. Insulin therapy
2. History of ketoacidosis or hyperosmolar hyperglycemic non-ketotic syndrome in the previous 6 months
3. Estimated glomerular filtration rate (eGFR) <60 mL/min by the MDRD equation
4. Alanine aminotransferase or aspartate aminotransferase >2.5 times the upper normal limit
5. Congestive heart failure (grade III-IV according to the New York Heart Association Criteria 1994)
6. Uncontrolled hypertension
7. Diabetic polyneuropathy, peripheral macrovascular pathology or diabetic foot
8. Proliferative diabetic retinopathy or severe nonproliferative diabetic retinopathy
9. History of stroke, transient ischemic attack or acute myocardial infarction in the previous 5 years
10. Recent surgery or acute infection in the previous 3 months
11. Major psychiatric disorder affecting compliance
12. Use of antipsychotic medications
13. Use of anticoagulant medications
14. Uncontrolled thyroid disorders
15. Systemic use of glucocorticoid steroids within previous 6 weeks
16. Osteoarticular or neurologic conditions able to limit physical activity
17. Cancer diagnosis or treatment in the past 5 years, with the exception of cancers that have been cured, and carry a good prognosis
18. Regular alcohol intake >2 portions per day
19. HIV positive
20. Pregnant or lactating women
21. Taken vitamin-mineral supplements during the previous 3 months

Date of first enrolment
18/07/2016

Date of final enrolment
06/08/2019

Locations

Countries of recruitment
Chile

Study participating centre
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Sponsor information

Organisation
University of Chile, Faculty of Medicine

ROR
https://ror.org/047gc3g35

Funder(s)

Funder type
Government

Funder Name
Fondo Nacional de Desarrollo Científico y Tecnológico Research project 1160792

Alternative Name(s)
National Fund for Scientific and Technological Development, El Fondo Nacional de Desarrollo Científico y Tecnológico, FONDECYT

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Chile

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available, but may be available on request after the study is complete and results have been analysed and published.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes