**CLINICAL TRIAL**

**Title of RCT:** The effects of Mediterranean diet with or without intermittent fasting in Type 2 Diabetes (the MedDietFast trial)

**Scientific Area:** Life Sciences (Medical & Health Sciences)

**Scientific field/s:** Medicine/Clinical Nutrition

**Trial design:**  A **3-arm parallel randomized single blind clinical trial** with an alternative dietary plan applied to patients with Type 2 Diabetes. The 3 arms will be as follows; a. control group, b. low saturated fat (<7% of TEI), high fiber (>40g/day) Mediterranean diet (MD) (Intervention I) and c. low saturated fat (<7% of TEI), high fiber (>40g/day) MD accompanied by time restricted feeding (TRF) (Intervention II). The active trial duration will be 6 months with follow-up in 2 weeks, 3 months, 4 months and 6 months since baseline.

**Main Goal & Objectives**

The objective of the present trial is associated with dietary interventions in the management of Type 2 Diabetes. The focus will be oriented towards the role of Mediterranean diet and a hot and unexplored topic in clinical nutrition regarding “intermittent fasting” and more specifically, “time restricted feeding” in diabetes patients. The **research hypothesis** is whether a Mediterranean dietary pattern with or without intermittent fasting may better control diabetes, as compared with a usual care diet. The **objectives** of the project are as follows; **a.** the superiority or non-inferiority of a MD accompanied by intermittent fasting vs. a MD and a conventional diet against Type 2 diabetes markers, **b.** the feasibility/sustainability of an intermittent fasting protocol, with moderate intensity, or standard healthy dietary patterns (i.e. Mediterranean, usual care diet) in patients with Type 2 Diabetes, **c.** the “clear” effect of “intermittent fasting” on diabetes markers, **d.** the design of an alternative dietary intervention for the management of diabetes mellitus, **e.** the reveal of more robust evidence regarding the effect of Mediterranean diet in the management of Type 2 diabetes.

|  |
| --- |
| **Table 1.** Inclusion and exclusion criteria |
| **Inclusion criteria** |
| 1. Informed consent |
| 2. Diagnostic criteria: Type 2 Diabetes (previously diagnosed with HbA1c >7.0% [53 mmol/mol] and/or taking antiglycemic medication) |
| **Exclusion criteria** |
| 1.Age <20 or >75 years old |
| 2.Body mass index<18 and >40kg/m2 |
| 3.Type 1 diabetes |
| 4. Liver abnormalities (ALT, AST, GGT>2.5 times the normal upper limit), proteinuria (urinary albumin to-creatinine ratio >30 mg/mmol); , impaired renal function eGFR<60, any significant endocrinopathy (other than stable treated thyroid disease), history of malignancy (other than nonmelanoma), liver, respiratory, gastrointestinal, or cardiovascular disease; pregnancy or lactation; clinical depression; history of/or current eating disorder; food allergies, coeliac disease; smoking. |

**Intervention:** The three arms of the clinical trial and the applied interventions are more extensively presented as follows; ***Control group****:* Participants randomised to the control group will receive intensive dietary counselling based on the Australian Dietary Guidelines for healthy eating ; ***Intervention I****:* intensivedietary counseling based on a MD, consumed ad libitum. Dietary recommendations: Vegetables: >500gr of non-starchy vegetables/day; fruits: > 2 fruits/day; legumes: >500g cooked legumes/week; red meat: 120-150g red meat fortnightly; poultry: 150g poultry/week; fish: 400-600g fish/week; dairy: low fat yogurt, skimmed milk, cheese < 90g (3x30g) feta cheese/week, eggs: <2 egg yolks / week; whole grains: whole wheat, rye, spelt flour, barley, oats; rice: long grain brown or basmati rice; pasta: preferably whole wheat and cooked al dente; pseudocereal: buckwheat, quinoa, amaranth; nuts/seeds: daily consumption; 1 tbsp flaxseed meal/day; alcohol for drinkers: 1 standard drink for women, 2 standard drinks for men (always with meals) at least 4 alcohol free days per week; main added fat: extra virgin olive oil; water: >5 glasses/day; elimination of white flour, sugar, soft drinks, juices and fried food; honey in small amounts. ***Intervention II****:* intensive dietary counseling based on a MD consumed ad libitum accompanied by TRF (12h fasting every day).Patients in all interventions will be provided with detailed information sheets, according to the intervention they are assigned to. Physical activity level will be estimated (translated, validated “International Physical Activity Questionnaire” short version). ***Compliance with intervention****:* to achieve compliance, each patient will have the same clinical nutritionist during the whole intervention. Participants will visit a Dietitian biweekly for 12 weeks and monthly thereafter to facilitate compliance. The absence of energy deficit, the moderate intensity of “fasting protocol” and the personalized sessions are also believed to enhance the level of compliance.

**Measurements at baseline and follow-up**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Examined parameters** | **0** | **W6** | **W12** | **W24** |
| Basic sociodemographic and clinical characteristics (interview) | x | - | - | - |
| Weight loss/weight gain/maintenance | - | x | x | x |
| Adherence to the intervention | - | x | x | x |
| Anthropometric measurements (body weight, height, waist circumference, waist to hip ratio) | x | x | x | x |
| Physical activity questionnaire | x | x | x | x |
| Systolic and diastolic blood pressure | x | x | x | x |
| Glycemic profile (HbA1, fasting glucose, plasma insulin concentrations) | x | - | x | x |
| Lipid profile (i.e total cholesterol, LDL, HDL, TGL, non-HDL) | x | - | x | x |
| Inflammatory markers (CRP) | x | - | x | x |
| Medication changes | x | x | x | x |
| Metabolites | x | x | x | x |

A major challenge for nutrition behavioral clinical trials is to suggest a dietary plan being not only in accordance with the recent literature tendency and showing promising results during the trial’s setting, but, most importantly, feasible to be adopted by the individuals in their daily life. The aim of the trial is to provide a feasible and sustainable guide to healthy eating, because it includes dietary guidelines based on the Mediterranean diet, combined with an innovative promising dietary protocol (Mediterranean diet accompanied by time restricted feeding), which can easily be adopted.