Clinical Nutrition ESPEN xxx (2017) e1–e6

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Randomized Controlled Trial

Green tea extract outperforms metformin in lipid profile and glycaemic control in overweight women: A double-blind, placebo-controlled, randomized trial

Monallisa Alves Ferreira, Anna Paula Oliveira Gomes, Ana Paula Guimarães de Moraes, Maria Luiza Ferreira Stringhini, João Felipe Mota, Alexandre Siqueira Guedes Coelho, Patrícia Borges Botelho*

Clinical and Sports Nutrition Research Laboratory (Labince), Faculty of Nutrition, Federal University of Goias, 74.605-080 Goiania, GO, Brazil

ARTICLE INFO

Article history:
Received 10 May 2017
Accepted 15 August 2017

Keywords:
Camellia sinensis
Metformin
Insulin resistance
Obesity
Lipoproteins LDL

SUMMARY

Background & aims: Both green tea and metformin are used as adjuvants to treat and prevent complications associated with obesity; however, studies comparing their action and interaction in non-diabetic overweight women have not been reported. Thus, the current study evaluated the effects of green tea extract and metformin, both individually and in combination, on type 2 diabetes risk factors in non-diabetic overweight women.

Methods: A total of 120 overweight women were randomly assigned in a double-blind manner to 1 of 4 groups, as follows: control ($n = 29$; 1 g of cellulose), green tea ($n = 32$; 1 g of dry green tea extract), metformin ($n = 28$; 1 g of metformin), and green tea + metformin ($n = 31$; 1 g of dry green tea extract + 1 g of metformin). Each group took the indicated capsules daily for 12 weeks. Anthropometric measurements, body composition, and fasting blood samples were evaluated.

Results: Although no significant interactions were observed in glycaemic control ($p = 0.07$), green tea in the absence of metformin reduced fasting glucose (-4.428 ± 2.00; $p = 0.031$), but when combined the lowering effect was nullified. In contrast, metformin increased HbA1c concentration ($0.048 \pm 0.189\%$; $p = 0.017$) and also reduced body weight (-1.318 ± 0.366 kg; $p = 0.034$) and LM (lean mass) (-1.249 ± 0.310; $p = 0.009$). Regarding lipid parameters, green tea significantly reduced total cholesterol and LDL-c.

Conclusions: Green tea was superior to metformin in improving glycaemic control and lipid profile in non-diabetic overweight women and, therefore, green tea extract is a promising alternative for reducing type 2 diabetes risk in overweight women.

1. Introduction

Obesity is correlated with disturbances in pancreatic islets, uncompensated glycaemic control and impaired glucose tolerance, all of which increase type 2 diabetes mellitus (DM2) risk [1]. Studies show that lifestyle changes can delay or prevent DM2 in individuals with obesity. In some cases, pharmacological interventions with oral antidiabetic agents such as metformin have been used to minimize DM2 risk even in non-diabetic obese patients [2]. However, in a crossover study with non-diabetic obese women, metformin did not improve blood glucose as expected [3]. Also, lifestyle changes may be equal to or more effective than metformin in treating abnormal glucose levels [4].

Abbreviations: LM, lean mass; FM, fat mass; PC, placebo group; GT, group receiving green tea extract supplementation alone; MF, group receiving metformin alone; GTMF, group receiving both green tea and metformin; Tea 0, groups receiving only metformin and/or placebo; Tea 1, group receiving green tea extract supplementation alone + group receiving green tea extract and metformin combined; Met 0, groups receiving green tea extract alone and/or placebo; Met 1, group receiving metformin alone + group receiving green tea extract and metformin combined.

* Corresponding author. Faculty of Nutrition, Federal University of Goiás, St. 227, Block 68, Setor Leste Universitário, 74.605-080 Goiânia, GO, Brazil.
E-mail address: patriciaborges.nutri@gmail.com (P. Borges Botelho).

http://dx.doi.org/10.1016/j.clnesp.2017.08.008
2405-4577/

Furthermore, side effects related to regular use of metformin, such as diarrhoea and vomiting episodes, may lead to the discontinuation of treatment [5]. Additionally, the cost-effectiveness of long-term early pharmacologic treatment of overweight individuals who have not been diagnosed with pre-diabetes or DM2 is questionable [6].

Green tea possesses similar actions to metformin in controlling glucose production and uptake, which may be useful for the prevention and treatment of obesity-related complications [7]. Based on its activity, green tea can improve glycaemic control [8], reduce body fat [9] and ameliorate other risk factors for type 2 diabetes, such as lipid profile [10].

To the best of our knowledge, studies comparing the effects of metformin and green tea, both individually and in combination, on body composition and DM2 risk factors in humans are not available. Therefore, we conducted the current double-blind, placebo-controlled, randomized trial to assess the effects of a green tea extract and metformin, individually and in combination, on body composition, lipid profile, and insulin resistance in non-diabetic overweight women.

2. Subjects and methods

2.1. Materials

Green tea was analysed using high-performance thin-layer chromatography (HPTLC), and encapsulated in a specialized laboratory (Nathupharmus®, GO, Brazil). Each green tea capsule contained 500 mg of *Camellia sinensis* leaf extract (extracted with ethanol 80%), with 280 mg polyphenols, including catechins. Metformin was quantified using high-performance liquid chromatography (HPLC), and colourimetric method was used to quantify cellulose, which served as the placebo in our study. Each capsule contained 500 mg of metformin or cellulose microcrystalline.

2.2. Subjects

Power calculation was performed based on an anticipated change in glycated haemoglobin concentration mean (our primary outcome). The estimated effect size was set to 1% decrease from the values in the control group. With a variance of 1.5 $(\%)^2$, a power of 0.8 and a significance level of 0.05, an estimated 24 subjects in each group, were needed. We estimated 25% of dropout rate and initiated the study with 120 subjects.

Participants were recruited between June and August 2014 through assessments of clinical records from nutritional primary care facilities and the endocrinology clinic within the Clinical Hospital of Federal University of Goias, Brazil.

To assess this calculated population, a total of 191 women were screened by a questionnaire containing the inclusion criteria for the study: women aged 20–45 years with abnormal glucose concentrations evaluated by fasting blood glucose (>100 mg/dL) or glycated haemoglobin (≥5.7%) and BMI > 28.9 kg/m^2 or BMI > 27.5 kg/m^2 and HOMA-IR > 3.60 [11]. All these parameters were assessed in the beginning of the study through biochemical tests.

The exclusion criteria were as follows: use of insulin or glycaemia-lowering medication; any weight control treatment; clinical diagnosis of diabetes, kidney disease, liver disease, heart disease, hyperthyroidism or menopause; pregnancy or breast-feeding; and daily consumption of any kind of tea.

2.3. Study design and diet intake

A 12-week randomized, double-blind, placebo-controlled study was performed in accordance with the principles in the Declaration of Helsinki and Good Clinical Practice guidelines. Ethical approval was obtained from the Ethics Committee of Federal University of Goias (reference number 636.652). The trial was also registered at ensaiosclinicos.gov.br (clinical trial RBR-4bdwxs). All participants provided written informed consent to participate in this study after being informed of its design both orally and in writing.

The participants were randomized into four groups using the Unweighted Pair Group Method with Arithmetic Mean (UPGMA) method as follows: Placebo (PC), 4 capsules containing microcrystalline cellulose/day (1 g/day); Green tea (GT), 2 capsules containing dry extract of green tea/day (1 g/day; 560 mg polyphenols) + 2 capsules containing placebo/day; Metformin (MF), 2 capsules containing metformin (1 g/day) + 2 capsules containing placebo/day; Green Tea + Metformin (GTMF), 2 capsules containing dry extract of green tea/day(1 g/day; 560 mg polyphenols) + 2 capsules containing metformin/day (1 g/day). The participants were instructed to consume two capsules before breakfast and two capsules before lunch for better absorption of both compounds and nutrients. They were also instructed to maintain their normal lifestyle habits, including those related to diet and physical exercise, during the 12-week intervention.

All of the capsules had the same appearance. An independent research group not involved in the study was responsible for administering the supplements according to randomization protocol; thus, the investigators and participants were both blinded. The blinding code was provided to the investigators after statistical analysis was complete.

Adherence to treatment was assessed by counting the number of capsules remaining when the participants returned to the laboratory. To increase the compliance, all individuals received weekly short messages on their cell phones and phone calls.

Compliance with the consumption of foods was monitored through a 7-day food record questionnaire that included five weekdays and two weekend days. The records were subsequently evaluated by the research team to assure that the dietary information was complete and accurate. Then, data on food records were analysed using Nutriquanti® (2011, São Paulo, SP, Brazil).

2.4. Primary and secondary outcome measures

The primary outcome measure in this study was glycated haemoglobin concentration, and the secondary outcome measures were fasting glucose, lipid profile and body composition. We also explored measures of pancreatic activity (HOMAs). All endpoints were measured at baseline and at 12 weeks in all groups.

2.5. Side effects reported during the intervention

The side effects reported by the participants were classified into different categories as follows: gastrointestinal, welfare, colour and odour of urine, feeling of fullness, fluid intake, diarrhoea, nausea, headache, heartburn, dry mouth, and other.

2.6. Anthropometric measurements and body composition

All measurements were performed by the same operator, who followed standard procedures. Subject height was measured during the selection phase to the nearest 0.5 cm with a stadiometer (Model Standard, Sanny®). After voiding and while wearing light clothing, each participant's body weight was measured to the nearest 0.1 kg on a digital scale (Filizola®, Brazil). Waist circumference was measured on undressed subjects at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest.

DXA assessments of fat mass (FM), lean mass (LM) and body fat percentage were conducted using a General Electric Lunar Prodigy

Please cite this article in press as: Alves Ferreira M, et al., Green tea extract outperforms metformin in lipid profile and glycaemic control in overweight women: A double-blind, placebo-controlled, randomized trial, Clinical Nutrition ESPEN (2017), http://dx.doi.org/10.1016/j.clnesp.2017.08.008