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Effectiveness of Ginger in the Treatment of Type 2 Diabetes Mellitus: A Pilot Study of the Randomized Clinical Trial Type*

Theme: Evidence-based practices.

Contribution to the subject: The most relevant contribution of this study is evidencing that the use of ginger, in the indicated doses, has potential as an adjuvant phytotherapeutic agent in the treatment of Type 2 Diabetes, as well as it can favor the reduction of biomarkers that exert a direct influence on the metabolic control of the disease in question. In addition, for being effective, easily accessible and low-cost, it can serve as a complementary technology to be offered in the nurses' clinical practice, supporting the performance of these professionals in the Health Care Networks, promoting better coverage and access to health.

ABSTRACT

Objective: To analyze the effectiveness of ginger in the reduction of the glycemic, lipid and anthropometric levels in people with Type 2 Diabetes *Mellitus*. **Materials and method:** A double-blind pilot study of the randomized clinical trial type, conducted between October 2017 and January 2018. The inclusion criteria were as follows: individuals with type 2 diabetes, aged from 18 to 80 years old, us-

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ing oral antidiabetic drugs, and with glycated hemoglobin values between 7 % and 10 %. The participants were randomized and allocated in two different groups. In the experimental group, the participants used 1.2 g of ginger and, in the control group, 1.2 g of placebo. The primary outcome was the reduction in blood glucose. The reduction in the lipid and anthropometric levels was the secondary outcome. The intervention lasted four weeks. **Results:** A total of 21 participants were included in the study. The use of 1.2 g of ginger resulted in noticeable reductions in the anthropometric and lipid levels in 30 days of follow-up, but it did not reduce the glycemic levels. **Conclusions:** In this study, it was shown that ginger capsules, in doses of 1.2 g a day, can help to reduce anthropometric measures and lipid levels in the population under study; however, it had no effect on the glycemic levels.

KEYWORDS (Source: DeCS)

Type 2 diabetes mellitus; ginger; clinical trial; primary health care; complementary therapies.

*Efectividad del jengibre en el tratamiento de la diabetes mellitus tipo 2: estudio piloto del tipo ensayo clínico aleatorizado**

RESUMEN

Objetivo: analizar la efectividad del jengibre en la reducción de los niveles glicémicos, lipídicos y antropométricos de personas con diabetes mellitus tipo 2. **Materiales y método:** estudio piloto, del tipo ensayo clínico aleatorizado, doble ciego, llevado a cabo entre octubre de 2017 y enero de 2018. Los criterios de inclusión fueron los siguientes: personas con diabetes tipo 2, de 18 a 80 años de edad, en uso de antidiabéticos orales y con valores de hemoglobina glicada entre 7 % y 10 %. Los participantes fueron aleatorizados y asignados en dos grupos distintos. En el grupo experimental, los participantes usaron 1,2 g de jengibre y, en el de control, 1,2 g de placebo. El resultado primario fue la reducción de la glicemia. La reducción de los niveles lipídicos y antropométricos fue el resultado secundario. La intervención duró cuatro semanas. **Resultados:** 21 participantes formaron parte del estudio. El uso de 1,2 g de jengibre evidenció perceptibles reducciones de los niveles antropométricos y lipídicos en 30 días de seguimiento, pero no se mostró suficiente para reducir los niveles glicémicos. **Conclusiones:** en el estudio se demostró que cápsulas de jengibre, en dosis de 1,2 g por día, pueden ayudar a reducir medidas antropométricas y niveles lipídicos en la población del estudio, sin embargo, sin efecto en los niveles glicémicos.

PALABRAS CLAVE (Fuente: DeCS)

Diabetes mellitus tipo 2; jengibre; ensayo clínico; atención primaria de salud; terapias complementarias.

* El artículo es resultado de la tesis doctoral "Efeito do gengibre (Zingiber officinale) no controle glicêmico e lipêmico de pessoas com diabetes tipo 2: ensaio clínico randomizado duplo-cego controlado por placebo" ("Efecto del jengibre (Zingiber officinale) en el control glicémico y lipémico de personas con diabetes tipo 2: ensayo clínico aleatorizado doble ciego controlado por placebo"), presentada al Programa de Posgrado en Enfermería de la Universidade Federal do Ceará y financiada por el Consejo Nacional de Desarrollo Científico y Tecnológico, Grant: 310496/2017– 9. Disponible en: http://www.repositorio.ufc.br/handle/riufc/36485.

Efetividade do gengibre no tratamento do diabetes *mellitus* tipo 2: estudo-piloto do tipo ensaio clínico randomizado*

RESUMO

Objetivo: analisar a efetividade do gengibre na redução dos níveis glicêmicos, lipídicos e antropométricos de pessoas com diabetes *mellitus* tipo 2. **Materiais e método:** estudo-piloto, do tipo ensaio clínico randomizado, duplo-cego, realizado entre outubro de 2017 e janeiro de 2018. Os critérios de inclusão foram: pessoas com diabetes tipo 2, de 18 a 80 anos, em uso de antidiabéticos orais e com valores de hemoglobina glicada entre 7 % e 10 %. Os participantes foram randomizados e alocados em dois grupos distintos. No grupo experimental, os participantes usaram 1,2 g de gengibre e, no grupo controle, 1,2 g de placebo. O desfecho primário foi a redução da glicemia. A redução dos níveis lipídicos e antropométricos foi o desfecho secundário. A intervenção durou quatro semanas. **Resultados:** 21 participantes fizeram parte do estudo. O uso de 1,2 g de gengibre trouxe perceptíveis reduções dos níveis antropométricos e lipídicos em 30 dias de acompanhamento, mas não se mostrou suficiente para a redução dos níveis glicêmicos. **Conclusões:** neste estudo, mostrou-se que cápsulas de gengibre, em doses de 1,2 g por dia, podem ajudar a reduzir medidas antropométricas e níveis lipídicos na população estudada, no entanto sem efeito nos níveis glicêmicos.

PALAVRAS-CHAVE (Fonte: DeCS)

Diabetes *mellitus* tipo 2; gengibre; ensaio clínico; atenção primária à saúde; terapias complementares.

* Este artigo é derivado da tese de doutorado intitulada "Efeito do gengibre (Zingiber officinale) no controle glicêmico e lipêmico de pessoas com diabetes tipo 2: ensaio clínico randomizado duplo-cego controlado por placebo", apresentada ao Programa de Pós-Graduação em Enfermagem da Universidade Federal do Ceará e financiada pelo Conselho Nacional de Desenvolvimento Científico e Tecnológico, Grant: 310496/2017– 9. Disponível em: http://www.repositorio.ufc.br/handle/riufc/36485.

Introduction

Even after years of research, Type 2 Diabetes Mellitus (T2DM) is still characterized as one of the main chronic diseases in the world (1). When diagnosed with this disease, the patient generally presents metabolic dysregulations that require continuous and expensive care. Currently, the clinical treatment is mainly focused on pharmacological interventions. However, oral antidiabetic medications are commonly associated with unwanted adverse effects that lead to discontinuation of therapy or clinical inertia, influencing the chronicity degree of the disease (2).

With this in mind, a number of research studies have been developed in an attempt to incorporate strategies that can minimize the lack of medication adherence and improve glycemic control. Given the above, experts have highlighted the antidiabetic properties of food supplements traditionally used in different cultures around the planet. Among them, ginger (*Zingiber officinale*) stands out, which has been used both as a spice, especially in cooking, for its spicy acid flavor and unique aroma, and as herbal medicine in the treatment of arthritis, non-alcoholic fatty liver disease, primary dysmenorrhea, seasickness and oncological therapies (3).

In addition to that, evidence has shown that ginger has the potential to reduce glycemic levels in people with T2DM, as well as its complications, as it interacts with different molecular pathways involved in the genesis of the disease, such as the inhibition of several transcriptional pathways, lipid peroxidation, reduction of carbohydrate metabolizing enzymes, and activation of the capacity of the antioxidant enzymes and low-density lipoprotein receptors. This cascade of events is reflected in the increase in insulin synthesis, in the reduction of insulin resistance, and in the accumulation of fat, in addition to the protective effects against complications arising from diabetes (4-9).

A meta-analysis showed that ginger can be considered an effective and promising adjuvant in the treatment of T2DM, since it does not present important adverse events and has been beneficial in attenuating the glycemic, lipid or even anthropometric levels of people with the disease. Despite this, researchers continue to recommend new studies to explore the therapeutic capacity of this product (3). In Brazil, studies on this topic are scarce and, for this reason, the objective of this research was to analyze the effectiveness of ginger in reducing glycemic, lipid and anthropometric levels in people with T2DM.

Methods

Type of study

This is a double-blind and placebo-controlled pilot study of the randomized clinical trial type, conducted between October 2017 and January 2018 according to the CONSORT recommendations in a Basic Health Unit (BHU) in the city of Picos, Piauí, Brazil.

Population

The population consisted of 50 individuals with T2DM, registered and monitored in a BHU located in the urban area of the municipality, selected for convenience.

Selection criteria

The inclusion criteria were as follows: individuals aged between 18 and 80 years old; using oral antidiabetic medications; with glycated hemoglobin (HbA1c) between 7 % and 10 %; and with preserved cognitive functions. The age group was determined for the following reasons: 1) individuals over 18 years of age have a better understanding of the disease and could be aware of the relationship of the study; 2) individuals over 80 years old begin to show a decline in their cognitive functions and, in order not to record any bias in this regard, we decided to limit such condition. The participants' cognitive function was assessed by means of the Mini-Mental State Exam. The exclusion criteria were as follows: being allergic to ginger, being pregnant or lactating, being an alcohol or tobacco user, making use of insulin, having severe complications associated with T2DM (chronic kidney, ischemic, autoimmune, liver, severe cardiovascular, gastrointestinal and inflammatory diseases), and the use of ginger supplementation. In addition to that, discontinuity criteria were adopted, namely: hospitalization, having started insulin therapy and/or presenting an allergic reaction.

Definition of the sample

As this is a pilot study in which the researchers involved sought to evaluate the effectiveness and feasibility of the intervention proposal, in addition to estimating the sample size for a future study, the sample of this research was selected for convenience. Of the 50 patients recruited, only 41 were interested in participating and, of these, 17 were excluded for the following reasons: one used

daily ginger supplementation; one had ascites; one was on insulin therapy; three reported having severe heart problems, and 11 had HbA1C results < 7 %. Thus, 24 participants were randomized.

The patients were randomly allocated in parallel groups (1:1), one being the experimental (ginger) and the other the control (placebo), each one with 12 people. Randomization was performed based on the HbA1c levels, by a researcher external to the study, using the R software, version 3.1.1. Each number of the randomization sequence was placed inside an envelope, sealed and given to the lead researcher only at the time of vial delivery. In this study, the participants and the lead researcher were kept blind.

Data collection

Before recruitment was started, the researcher responsible for the study met with the team of the BHU chosen and clarified the research to the professionals. The potential participants were recruited over the course of 15 days, through printed invitations made by the researcher and delivered by community health agents. Day and time were scheduled so that patients could attend the BHU.

In addition to the BHU nurse, the responsible researcher was present to clarify the intention of the research and to invite the patients to participate. For those who showed interest, the Free and Informed Consent Form (FICF) was presented, signatures were collected, and the HbA1c test was collected at the site. After this stage, with the results in hand, the patients were instructed on the possibility of participating in the study. Data collection was conducted at the same moment for those who were able and wanted to participate.

For data collection, the questionnaire used included socioeconomic variables (gender, skin color, schooling, occupation, etc.), anthropometric variables (waist circumference, hip circumference, neck circumference, waist-hip ratio, body adiposity index, body mass index, thigh circumference, waist-to-height ratio), clinical variables (blood pressure, time since T2DM diagnosis, episodes of hypo/hyperglycemia in the 30 days prior to collection) and laboratory variables (capillary blood glucose — CBG, fasting blood glucose — FBG, low density lipoprotein — LDL, high density lipoprotein — HDL, total cholesterol — TC, and triglycerides — TG). First, in order to guarantee data uniformity, the responsible researcher trained the other Nursing students and professionals involved in data collection.

As for the anthropometric variables, body weight was measured on an empty stomach, with the participants wearing light clothes and without shoes. Height was also measured with the participants barefooted, using a stadiometer attached to the scale. The body mass index (BMI) was calculated using the weight-to-height ratio (kg/m^2), where < 18.5 kg/m^2 indicated low weight; between 18.5 kg/m^2 and 24.9 kg/m2, normal weight; between 25 kg/m^2 and 29.9 kg/m^2, overweight; and ≥ 30 kg/m^2, obesity. Aged patients were classified as underweight when BMI ≤ 22 kg/m^2, as with appropriate weight when BMI was between > 22 kg/m^2 and < 27 kg/m^2, and as overweight with BMI ≥ 27 kg/m^2 (10).

To measure neck circumference (NC), the participants were in a full standing position, with the head positioned in the Frankfurt horizontal plane. An inelastic tape was placed at the midpoint of the neck. In men, the measurement was taken just below the laryngeal prominence. NC was considered high when men presented values ≥ 39 cm, and ≥ 35 cm for women (11). Waist circumference (WC) was measured with an inelastic measuring tape placed against the skin, at the midpoint between the iliac crest and the last rib at the end of the exhalation movement. The WC measure was considered according to gender, with cutoff points ≤ 90 cm for men and ≤ 80 cm for women (11).

The hip circumference (HC) cutoff value was ≤ 100 cm for both genders (11). The waist-to-height ratio (WHtR) showed a cutoff value of 0.5 for both genders. With regard to the waist-to-hip ratio (WHR), the cutoff points were 0.8 for women and 1.0 for men (11). Regarding the body adiposity index (BAI), the values considered were 25 % for men and 35 % for women (12). Thigh circumference (ThC) was measured with an inelastic measuring tape, at the midpoint between the inguinal crease and the proximal edge of the patella, and the cutoff values were ≥ 44 cm for men and ≥ 43.70 cm for women (12).

To be considered hypertensive, the participants should have blood pressure values over 139/89 mmHg, according to the VII Brazilian Guideline on Arterial Hypertension. Below this value, they were classified as normotensive (13).

The laboratory data corresponded to the values established by the Brazilian Diabetes Society (14) and by the VI Brazilian Guideline on the Prevention of Dyslipidemias and Atherosclerosis (15), with FBG (≤ 100 mg/dL), HbA1c (< 7 %), TC (≤ 90 mg/dL),

TG (≤ 150 mg/dL), LDL (≤ 100 mg/dL) and HDL (≥ 40 mg/dL). 10 mL blood samples were collected after 12 to 14 hours of fasting. The samples were centrifuged at room temperature, at 3000 rpm for 10 minutes, to separate the serum from the blood cells. FBG, TG, TC, LDL, HDL, and HbA1c were determined by the enzymatic colorimetric method with commercially available kits (Pars Azmun Co., Tehran, Iran) in an automated analyzer (Abbott, Alcyon 300 model, Abbott Park, IL, USA).

In this study, the participants in the experimental group received 60 capsules of 600 mg/each, with ginger (*Zingiber officinale*). The CG participants received 60 capsules of 600 mg/each, with microcrystalline cellulose (placebo). All the participants were instructed to take two capsules a day, one 30 minutes before breakfast and another 30 minutes before dinner, daily, for 30 days. Both the ginger and the placebo were encapsulated and packaged in identical, opaque white plastic vials, properly sealed. Each vial was numbered, and the dosage and the participant's name were printed on its label. The experiment participants were carefully instructed to avoid changes in their physical activity routines or eating patterns during the study period.

All the participants were instructed to return after the 30 days of intervention. In addition to that, guidelines were given on the continuity of ingestion of medications for T2DM, prescribed by the physicians, and on the usual care for managing the disease. Although foreign studies prove a safety ginger dose of up to 6 g/day, in Brazil, the maximum dosages allowed in compounding pharmacies for daily consumption are 2 g for fresh ginger and 1.2 g for 0.1 % ginger dry extract. Thus, ginger dry extract was selected, in which the daily dose was distributed in two 600 mg capsules instead of fresh ginger, which would have its daily dose divided into four capsules.

For production of the ginger capsules, the rhizome was used, processed in the form of powder, and the final product was 0.1 % ginger dry extract. In addition to that, an extraction was performed with water as solvent and starch as excipient. Drying was done by spray dryer. As for the physical aspects, the concentration of the extract in water was 33.51 %, and alcohol, 0.89 %. Dosage was 0.36 % for total gingerols (6-gingerol, 10-gingerol, 6-shogaol). In addition to the physical-chemical test carried out by the manufacturer, a microbiological test was performed, with values within normality for the amount of bacteria, fungi and yeasts, and the purity test measured heavy metals such as lead, copper, and antimony.

The use of ginger is authorized in Brazil and does not require permission to be used in research studies. Therefore, the concept of "Access to the Genetic Heritage" available in Provisional Measure 2,186-16/2001 does not apply. It is worth remembering that this spice, despite being originally from the island of Java, Indonesia, is widely used in the tropical regions of the world.

After the purchase of 0.1 % ginger dry powdered extract by *Gemini Indústria de Insumos Farmacêuticos Ltda*, the weighing, encapsulation, and repetition of the quality control tests, such as the physical-chemical test, were carried out in a compounding pharmacy that has the green seal of quality, the seal of excellence in franchising, and the Sinamm Diploma. Weighing was computed using an analytical balance. The ginger and placebo capsules were prepared by a private laboratory, certified by the National Health Surveillance Agency, in compliance with the international standards for handling products and medications. After preparation, the capsules were analyzed by pharmacists associated with the Federal University of Piauí, through biochemical and toxicological tests. The primary outcome was the reduction in the levels of FBG and CBG. The reduction in the lipid and anthropometric levels was established as the secondary outcome.

Data analysis and treatment

The data were analyzed by intention to treat, by repeating the values of the last evaluation, according to the CONSORT recommendations. The confounding variables were minimized through randomization in parallel groups (1:1). For the scalar variables, data was presented as mean and standard deviation or as median, minimum, and maximum. In the categorical variables, data was presented in the form of frequency and prevalence rate, in order to investigate associations between risk factors and disease. The Mann-Whitney's U test was used to analyze the characteristics of the groups. To verify the behavior of the numerical variables, at both moments, the Wilcoxon test was used. A significance level of 5 % was adopted. Pearson's chi-square test or Fisher's exact test for categorical variables were used to investigate the association between the variables. The statistical analyses were performed with the Statistical Package for the Social Sciences software, version 22.0 (United States) and the R program, version 3.3.1.

Ethical aspects

The study was approved by a Research Ethics Committee under opinion No. 2017 (CAAE: 71423617.3.0000.5209), registered

in the Brazilian Network of Clinical Trials (RBR-2rt2wy / TRIAL: U111-1202-1650), and followed all the ethical recommendations of the Brazilian National Health Council, according to Resolutions 466/2012 and 580/2018. All the participants were informed about the benefits and risks of the study and were free to abandon it, at any time and for any reason.

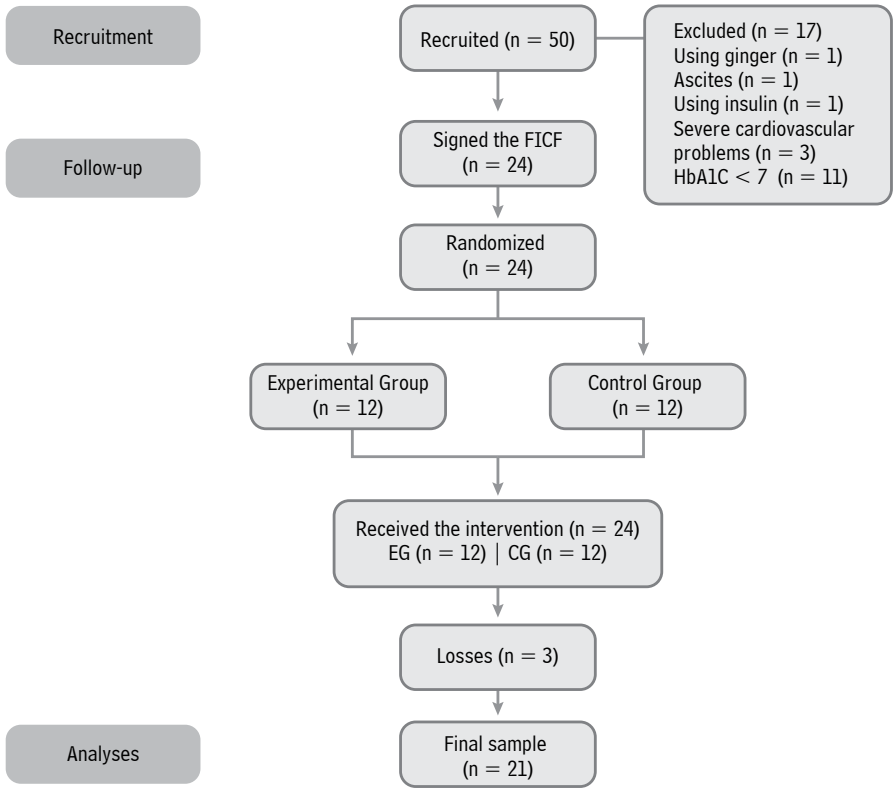
Results

A total of 24 participants received guidelines on the study, signed the FICF and were randomized, with 12 being allocated to the EG and the CG each. Subsequently, three EG participants were discontinued for the following reasons: two for travel reasons and one for reporting tachycardia. Thus, 21 individuals concluded the study (Figure 1).

Most of the patients were female (66.7 %), brown-skinned (66.7 %), and with a mean age of 57.9 years old (SD ± 9.22). The overall mean schooling of the participants was 6.95 years (SD ± 5.1) and 85.7 % lived with a partner or family members. One third of the participants stated being unemployed, received unemployment benefits or had the income of another family member, where 85.8 % had a monthly income of one to three minimum wages (value of the monthly minimum wage effective in 2017 in Brazil), and 85.7 % were married or in a stable union.

When asked about hyperglycemia or hypoglycemia episodes in the 30 days prior to the intervention, 66.7 % of the participants reported episodes of hyperglycemia and none of hypoglycemia. Almost half of the individuals (47.6 %) reported going to nursing and medical appointments every six months, and a large propor-

Figure 1. Flowchart of the participants involved in the study. Picos, Piauí, Brazil, 2017



Source: Own elaboration.

tion (76.23 ± 4.27) only measures glycemic and lipid levels twice a year. In this study, arterial hypertension was the disease most associated with T2DM (61.9 %). Of the research participants, only one reported heartburn as an adverse effect.

In Table 1, it can be seen that, after the intervention with ginger, the researchers did not identify significant differences in the percentage values of the variables analyzed.

As for the mean values of the anthropometric and laboratory variables, the participants who used ginger had reductions in weight (75.1-74.4/p = 0.021), BMI (29.5-29.3/p = 0.031), WC (100.8-99.7/p = 0.050), NC (36.7-36.1/p = 0.293), HC (105.0-104.4/p = 0.066), ThC (47.1-46.7/p = 0.483), BAI (33.41-32.92/p = 0.066), HDL (37.78-45.08/p = 0.086), and LDL (113.99-108.50/p = 0.038) (as well as a 95 % confidence interval) (Table 2).

Table 1. Distribution of the data of the patients with T2DM according to clinical, anthropometric and laboratory variables, before and after the intervention. Picos, Piauí, Brazil, 2017

Variables	Pre-intervention			p*	Post-intervention			p*
	Total	Ginger	Placebo		Total	Ginger	Placebo	
Blood pressure				0.661				0.397
Normal	12 (57.1 %)	06 (66.7 %)	06 (50 %)		14 (66.7 %)	05 (55.5 %)	09 (75 %)	
Hypertension	09 (42.8 %)	03 (33.3 %)	06 (50 %)		07 (33.3 %)	04 (44.5 %)	03 (25 %)	
BMI†				0.659				1
Eutrophic	06 (28.6 %)	02 (22.2 %)	04 (33.3 %)		05 (23.8 %)	02 (22.2 %)	03 (25 %)	
Overweight/Obesity	15 (71.4 %)	07 (77.8 %)	08 (66.7 %)		16 (76.2 %)	07 (77.8 %)	09 (75 %)	
WC				1				0.603
Normal	03 (14.3 %)	01 (11.1 %)	02 (16.7 %)		04 (19 %)	01 (11.1 %)	03 (25 %)	
Altered	18 (85.7 %)	08 (88.9 %)	10 (83.3 %)		17 (81 %)	08 (88.9 %)	09 (75 %)	
NC				0.331				0.397
Normal	06 (28.6 %)	04 (44.4 %)	02 (16.7 %)		07 (33.3 %)	04 (44.4 %)	03 (25 %)	
Altered	15 (71.4 %)	05 (55.6 %)	10 (83.3 %)		14 (66.7 %)	05 (55.6 %)	09 (75 %)	
HC				1				1
Normal	07 (33.3 %)	04 (33.3 %)	03 (33.3 %)		08 (38.1 %)	05 (41.7 %)	03 (33.3 %)	
Altered	14 (66.7 %)	08 (66.7 %)	06 (66.7 %)		13 (61.9 %)	07 (58.3 %)	06 (66.7 %)	
ThC				1				1
Normal	02 (09.5 %)	01 (11.1 %)	01 (8.3 %)		02 (09.5 %)	01 (11.1 %)	01 (08.3 %)	
Altered	19 (90.5 %)	08 (88.9 %)	11 (91.7 %)		19 (90.5 %)	08 (88.9 %)	11 (91.7 %)	
WHR				1				1
Normal	06 (28.6 %)	03 (33.3 %)	03 (25 %)		07 (33.3 %)	03 (33.3 %)	04 (33.3 %)	

Variables	Pre-intervention			p*	Post-intervention			p*
	Total	Ginger	Placebo		Total	Ginger	Placebo	
Altered	15 (71.4 %)	06 (66.7 %)	09 (75 %)		14 (66.7 %)	06 (66.7 %)	08 (66.7%)	
BAI‡				0.367				0.642
Normal	08 (38.1 %)	02 (22.2 %)	06 (50 %)		07 (33.3 %)	02 (22.2 %)	05 (41.7 %)	
Altered	13 (61.9 %)	07 (77.8 %)	06 (50 %)		14 (66.7 %)	07 (77.8 %)	07 (58.3%)	
NTR				1				0.486
Normal	01 (4.8 %)	01 (8.3 %)	-		02 (9.5 %)	02 (16.7 %)	-	
Altered	20 (95.2 %)	11 (91.7 %)	09 (100 %)		19 (90.5 %)	10 (83.3 %)	09 (100 %)	
Capillary blood glucose				1				0.229
Normal	-	-	-		03 (14.3 %)	-	03 (25 %)	
Altered	21 (100 %)	09 (100 %)	12 (100 %)		18 (85.7 %)	09 (100 %)	09 (75 %)	
Fasting blood glucose				1				0.229
Normal	-	-	-		03 (14.3 %)	-	03 (25 %)	
Altered	21 (100 %)	09 (100 %)	12 (100 %)		18 (85.7 %)	09 (100 %)	09 (75 %)	
Total cholesterol				0.396				1
Normal	09 (42.9 %)	05 (55.6 %)	04 (33.3 %)		05 (23.8 %)	02 (22.2 %)	03 (25 %)	
Altered	12 (57.1 %)	04 (44.4 %)	08 (66.7 %)		16 (76.2 %)	07 (77.8 %)	09 (75 %)	
HDL				0.087				1
Normal	12 (57.1 %)	03 (33.3 %)	09 (75 %)		15 (71.4 %)	06 (66.7 %)	09 (75 %)	
Altered (low)	09 (42.9 %)	06 (66.7 %)	03 (25 %)		06 (28.6 %)	03 (33.3 %)	03 (25 %)	
LDL				1				0.673
Normal	06 (28.6 %)	03 (33.3 %)	03 (25 %)		08 (38.1 %)	04 (44.4 %)	04 (33.3 %)	
Altered	15 (71.4 %)	06 (66.7 %)	09 (75 %)		13 (61.9 %)	05 (55.6 %)	08 (66.7 %)	
Triglycerides				1				0.553
Normal	04 (19 %)	02 (22.2 %)	02 (16.7 %)		03 (14.3 %)	02 (22.2 %)	01 (08.3 %)	
Altered	17 (81 %)	07 (77.8 %)	10 (83.3 %)		18 (85.7 %)	07 (77.8 %)	11 (91.7 %)	

* Fisher's exact test; †Body Mass Index; ‡Body Adiposity Index.

Source: Own elaboration.

Table 2. Distribution of the mean values of the patients with T2DM, according to clinical, anthropometric and laboratory variables, before and after the intervention. Picos, Piauí, Brazil, 2017

Variables	Placebo			Ginger		
	Pre-intervention	Post-intervention	p*	Pre-intervention	Post-intervention	p*
Systolic pressure	122.5 (100 - 165)	120 (105 - 160)	0.514	125 (99 - 175)	125 (104 - 140)	0.362
Diastolic pressure	75 (70 - 100)	76 (66 - 110)	0.959	80 (70 - 100)	80 (70 - 91)	0.205
Weight	70.5 (59.2 - 95.7)	69.8 (57.8 - 97.1)	0.108	75.1 (46 - 90.3)	74.4 (46.3 - 89.5)	0.021
BMI†	27 (22.8 - 34.2)	27 (22.3 - 34.3)	0.283	29.5 (20.4 - 34.8)	29.3 (20.6 - 34.5)	0.031
WC‡	99 (81 - 109.9)	97.1 (78.7 - 114.5)	0.050	100.8 (79 - 106)	99.7 (78.7 - 105.5)	0.050
NC§	37.6 (33.9 - 41.9)	37.7 (33.7 - 43.5)	0.220	36.7 (32.6 - 44.9)	36.1 (32.6 - 45.5)	0.293
HC||	103.3 (94 - 114.8)	103.6 (93 - 115.1)	0.306	105 (88.2 - 120)	104.5 (88.4 - 120.6)	0.066
ThC¶	47.5 (38.9 - 50.9)	47.1 (40.7 - 52)	0.388	47.1 (37.3 - 60)	46.7 (37.7 - 58.7)	0.483
WHR**	0.9 (0.7 - 1.0)	0.9 (0.7 - 1)	0.106	0.9 (0.8 - 1)	0.9 (0.8 - 1)	0.236
BAI††	32.3 (24.9 - 49.8)	31.5 (24.2 - 50)	0.306	33.4 (29.9 - 47)	32.9 (29.8 - 46.4)	0.066
WHtR‡‡	0.6 (0.5 - 0.7)	0.5 (0.48 - 0.69)	0.093	0.6 (0.52 - 0.71)	0.6 (0.5 - 0.71)	0.577
Capillary blood glucose	243 (144 - 360)	216 (142.2 - 345.6)	0.754	203.4 (131.4 - 306)	207 (111.6 - 253.8)	0.953
Fasting blood glucose	223.2 (135 -369)	226.8 (136.8 - 363.6)	0.844	198 (117 -318.6)	223.2 (111.6 - 261)	0.859
Total cholesterol	235.8 (139.2 - 309.3)	204.9 (139.2 - 278.4)	0.480	185.6 (123.7 - 282.2)	197.2 (135.3 - 239.7)	0.953
HDL	46.4 (19.3 - 65.7)	50.2 (30.9 - 65.7)	0.239	34.8 (23.2 - 69.6)	42.5 (30.9 - 61.8)	0.086
LDL	135.3 (65.7 - 587.7)	112.1 (69.6 -165.8)	0.071	112.1 (69.6 -185.6)	108.2 (42.5 -131.4)	0.038
Triglycerides	186 (79.7 -345.4)	203.7 (106 -354.2)	0.347	194.3 (115.1-504.8)	248 (124 -575.7)	0.260

* Wilcoxon Test; †Body Mass Index; ‡Waist Circumference; §Neck Circumference; ||Hip Circumference; ¶Thigh Circumference; **Waist-to-Hip Ratio; ††Body Adiposity Index; ‡‡Waist-to-Height Ratio.

Source: Own elaboration.

Discussion

The results of this study showed that the daily intake of 1.2 g of ginger reduced weight, BMI, WC and LDL in 30 days of follow-up. Studies that used ginger in people with T2DM, with a focus on reducing blood sugar levels, also found positive results in reducing the anthropometric levels (weight, BMI and WC) (16-19). Although directly linked to the diagnosis of T2DM, changes in the anthropometric levels — caused by the accumulation of fat — are still poorly investigated in studies that address the use of ginger.

In this research, although ginger has improved the lipid profile ranges, such as LDL (112.14-108.27 mg/dL, p = 0.038) and

HDL (34.08-42.53 mg/dL, p = 0.086), there was no unanimity in the consistency of the individual results. A similar study, involving 80 people with T2DM, with 41 using 3 g/day of ginger, for eight weeks, concluded that the product reduces LDL levels and increases HDL levels (17). Iranian researchers conducted a clinical trial with 64 patients for two months, in which the participants used 2 g/day of ginger and achieved a reduction in the mean LDL values (77.33-65.73 mg/dL, p = 0.04). However, when analyzing the impact on HDL, the results were negative, as the levels of this cholesterol decreased (42.53-38.66 mg/dL, p = 0.28) (16). Amounts of ginger smaller than these have not been shown to be effective in reducing the lipid levels (20).

Results like these are important, since it is already firmly established in the literature that insulin resistance in the peripheral tissues is intimately associated to the high amount of circulating lipids and to the accumulation of tissue lipids, which indicates a high need for control, essential to minimize secondary complications of T2DM and of associated diseases (21). Ginger has enzymes that inhibit the metabolism of carbohydrates, preventing hyperglycemia or the perpetuation of insulin resistance, and appears to modulate the action of insulin while regulating blood glucose homeostasis (21).

Although the results did not show that fasting blood glucose or capillary blood glucose were reduced after the intervention, different studies highlight the hypoglycemic effect of ginger in non-insulin-dependent T2DM patients (17-18, 22-27). The outcomes of this study and others with a similar objective can be supported by differences in the patients' responses, the duration of the disease, the dose, the intervention time or because of the type of therapeutic regimen. In general, all this evidence shows that the consumption of a moderate dose of ginger can modify the glycemic and lipid status, and reduce the anthropometric parameters of people with diabetes, pointing out the value of the product in the management of the disease. Thus, it is possible to say that ginger can even be used as an adjunct, but not exclusive, therapy for the control of T2DM. In addition to that, it is important to note that ginger is a low-cost product, easily found and with great potential to be introduced into the daily lives of people with T2DM and comorbidities associated with lipid alteration.

Undoubtedly, the results of research studies like this support the health team in the use of products like ginger in the clinical practice, increasing the management power of people with T2DM, especially in primary care. Likewise, it is also necessary to take into account that the current scenario requires greater autonomy, preparation and leadership from these professionals in the creation of policies that disseminate effective and innovative practices, as highlighted by the Nursing Now campaign (28-30).

Based on our observations and on data from other research studies, it is possible that ginger is considered a promising supplement for T2DM therapy when hypertriglyceridemia and hyperlipidemia cannot be satisfactorily controlled by means of other strategies, such as exercise, diet and prescription medications. A research study on the cost-effectiveness of the product is also important, since the use of ginger can be part of the economic and health strategies used by the Brazilian government to control T2DM.

Study limitations

As a limitation of this pilot study we point out the intervention time, of only 30 days, which seems to be short to show metabolic changes in patients with diabetes, as well as the sample size, precluding data generalization. Another limitation of the research was the therapeutic dose of only 1.2 g per day — the maximum dose allowed by the Brazilian government. In addition to that, the need to monitor and record the dietary pattern and the practice of physical exercises by the participants is emphasized, since they can influence the outcomes found.

Conclusions

This study identified that ginger, in doses of 1.2 g/day, for 30 days, can help to reduce some anthropometric and lipid levels in people with T2DM, but it does not have enough hypoglycemic power to reduce the investigated glycemic levels. In addition to that, inconsistencies found in the literature, with positive and negative results in studies of this nature, raise the need for further research studies. Therefore, caution is required when using the results. Nurses must lead research studies like this, as they are at the forefront of care for people with T2DM, especially in primary care. In addition, policy makers are expected to expand the list of recommendations for this product and to provide opportunities for developing new studies that take into account the limiting aspects of this research, especially the size of the daily therapeutic dose.

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References

1. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet Diabetes Endocrinol [internet]. 2017; 389:2239-51. DOI: http://dx.doi.org/10.1016/S0140-6736(17)30058-2

2. Khunti K, Nikolajsen A, Thorsted BL, Andersen M, Davies MJ, Paul SK. Clinical inertia in intensifying therapy among people with type 2 diabetes treated with basal insulin. Diabetes Obes Metab [internet]. 2016; 8:401-9. DOI: https://doi.org/10.1111/dom.12626

3. Zhu J, Chen H, Song Z, Wang X, Sun Z. Effects of ginger (*Zingiber officinale roscoe*) on Diabetes Mellitus Type 2 and components of the metabolic syndrome: A systematic review and meta-analysis of randomized controlled trials. Evid Based Complement Alternat Med [internet]. 2018; 2018:5692962. DOI: https://doi.org/10.1155/2018/5692962

4. Huang F-Y, Deng T, Meng L-X, Ma X-L. Dietary ginger as a traditional therapy for blood sugar control in patients with type 2 diabetes mellitus: A systematic review and meta-analysis. Medicine (Baltimore) [internet]. 2019; 98(13):e15054. DOI: https://doi.org/10.1097/MD.0000000000015054

5. Wang J, Ke W, Bao R, Hu X, Chen F. Beneficial effects of ginger Zingiber officinale Roscoe on obesity and metabolic syndrome: A review. Ann N Y Acad Sci [internet]. 2017; 1398(1):83-98. DOI: https://doi.org/10.1111/nyas.13375

6. Honarvar NM, Zarezadeh M, Khorshidi M, Arzati MM, Yekaninejad MS, Abdollahi M *et al.* The effect of an oral ginger supplementation on NF-kB concentration in peripheral blood mononuclear cells and anthropomorphic data of patients with type 2 diabetes: A randomized double-blind, placebo-controlled clinical trial. Complement Ther Med [internet]. 2019; 42:7-11. DOI: https://doi.org/10.1016/j.ctim.2018.10.019

7. Kiyama R. Nutritional implications of ginger: Chemistry, biological activities and signaling pathways. J Nutr Biochem [internet] 2020; 86:108486. DOI: https://doi.org/10.1016/j.jnutbio.2020.108486

8. Wang Y, Yu H, Zhang X, Feng Q, Guo X, Li S *et al.* Evaluation of daily ginger consumption for the prevention of chronic diseases in adults: A cross-sectional study. Nutrition [internet]. 2017; 36:79-84. DOI: https://doi.org/10.1016/j.nut.2016.05.009

9. Rahimlou M, Yari Z, Rayyani E, Keshavarz SA, Hosseini S, Morshedzadeh N *et al.* Effects of ginger supplementation on anthropometric, glycemic and metabolic parameters in subjects with metabolic syndrome: A randomized, double-blind, placebo-controlled study. J Diabetes Metab Disord [internet] 2019; 18(1):119-25. DOI: https://doi.org/10.1007/s40200-019-00397-z

10. Lipschitz DA. Screening for Nutritional Status in the Elderly. Prim Care [internet]. 1994; 21(1):55-67. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8197257

11. Vasques AC, Rosado L, Rosado G, Ribeiro RC, Franceschini S, Geloneze B. Anthropometric indicators of insulin resistance. Arq Bras Cardiol [internet]. 2010; 95(1):14-23. Available from: http://www.scielo.br/pdf/abc/v95n1/en_a25v95n1.pdf

12. Segheto W, Hallal PC, Marins JCB, da Silva DCG, Coelho FA, Ribeiro AQ *et al.* Factors associated with body adiposity index (BAI) in adults: Population-based study. Cien Saude Colet [internet]. 2018; 23(3):773-83. DOI: http://doi.org/10.1590/1413-81232018233.11172016

13. Setiati S, Istanti R, Andayani R, Kuswardhani RA, Aryana IG, Putu ID, Apandi M, Inchwani J, Soewoto S, Dinda R, Mustika S. Cut-off of Anthropometry measurement and nutritional status among elderly outpatient in Indonesia: Multicentre study. Acta Med Indones [internet]. 2010; 42(4):224-30. Available from: http://www.inaactamedica.org/archives/2010/21063044.pdf

14. Malachias MVB, Souza WKSB, Plavnik FL, Rodrigues CIS, Brandão AA, Neves MFT *et al.* VII Brazilian guidelines for hypertension. Arq Bras Cardiol [internet]. 2016; 107(3):1-83. Available from: http://publicacoes.cardiol.br/2014/diretrizes/2016/05_HIPERTENSAO_ARTERIAL.pdf

15. Brazilian Diabetes Society. Guidelines from the Brazilian Diabetes Society: 2017-2018 [internet]. 2017. Available from: https://www.diabetes.org.br/profissionais/images/2017/diretrizes/diretrizes-sbd-2017-2018.pdf

16. Faludi AA, Izar MCO, Saraiva JFK, Chacra APM, Bianco HT, Afiune Neto A *et al*. Atualização da Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose — 2017. Arq Bras Cardiol [internet]. 2017; 109(2 suppl 1):1-76. Disponível em: http://publicacoes.cardiol.br/2014/diretrizes/2017/02_DIRETRIZ_DE_DISLIPIDEMIAS.pdf

17. Mahluji S, Attari VE, Mobasseri M, Payahoo L, Ostadrahimi A, Golzari SE. Effects of ginger (*Zingiber officinale*) on plasma glucose level, HbA1c and insulin sensitivity in type 2 diabetic patients. Int J Food Nutr [internet]. 2013; 64(6):682-6. DOI: http://doi.org/10.3109/09637486.2013.775223

18. Azimi P, Ghiasvand R, Feizi A, Hariri M, Abbasi B. Effects of cinnamon, cardamom, saffron, and ginger consumption on markers of glycaemic control, lipid profile, oxidative stress, and inflammation in type 2 diabetes patients. Rev Diabet Stud [internet]. 2014; 11(3-4):258-66. DOI: http://doi.org/10.1900/RDS.2014.11.258

19. Mozaffari-Khosravi H, Talaei B, Jalali BA, Najarzadeh A, Mozayan MR. The effect of ginger powder supplementation on insulin resistance and glycaemic indices in patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial. Complement Ther Med. [internet]. 2014; 22(1):9-16. DOI: http://doi.org/10.1016/j.ctim.2013.12.017

20. Shidfar F, Rajab A, Rahideh T, Khandouzi N, Hosseini S, Shidfar S. The effect of ginger (*Zingiber officinale*) on glycaemic markers in patients with type 2 diabetes. J Complement Integr Med [internet]. 2015; 12(2):165-70. DOI: http://doi.org/10.1515/jcim-2014-0021

21. Atashak S, Peeri M, Azarbayjani MA, Stannard SR, Haghighi MM. Obesity-related cardiovascular risk factors after long-term resistance training and ginger supplementation. J Sports Sci Med [internet]. 2011; 10(4):685-91. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3761505/pdf/jssm-10-685.pdf

22. Li Y, Tran VH, Duke CC, Roufogalis BD. Preventive and protective properties of zingiber officinale (ginger) in diabetes mellitus, diabetic complications, and associated lipid and other metabolic disorders: A brief review. Evid Based Complement Alternat Med. [internet]. 2012; 2012:516870. DOI: http://doi.org./10.1155/2012/516870

23. Al-Amin ZM, Thomson M, Al-Qattan KK, Peltonen-Shalaby R, Ali M. Anti-diabetic and hypolipidaemic properties of ginger (*Zingiber officinale*) in streptozotocin-induced diabetic rats. Br J Nutr [Internet]. 2006; 96(4):660-6. DOI: http://doi.org/10.1079/BJN20061849

24. Ozougwu JC, Eyo JE. Evaluation of the activity of *Zingiber officinale* (ginger) aqueous extracts on alloxan-induced diabetic rats. Pharmacologyonline [internet]. 2011; 1:258-69. Available from: https://pharmacologyonline.silae.it/files/archives/2011/vol1/026.ozougwu.pdf

25. Kazeem MI, Akanji MA, Yakubu MT, Ashafa AOT. Protective effect of free and bound polyphenol extracts from ginger (*Zingiber officinale Roscoe*) on the hepatic antioxidant and some carbohydrate metabolizing enzymes of streptozotocin-induced diabetic rats. Evid Based Complement Alternat Med [internet]. 2013; 2013:935486. DOI: http://doi.org/10.1155/2013/935486

26. Oludoyin AP, Adegoke SR. Efficacy of ginger (*Zingiber officinale Roscoe*) extracts in lowering blood glucose in normal and high fat diet-induced diabetic rats. Am J Food Nutr [internet]. 2014;2(4):55-8. Available from: http://pubs.sciepub.com/ajfn/2/4/1/index.html

27. Arablou T, Aryaeian N, Valizadeh M, Sharifi F, Hosseini AF, Djalali M. The effect of ginger consumption on glycemic status, lipid profile and some inflammatory markers in patients with type 2 diabetes mellitus. Int J Food Sci Nutr [internet]. 2014; 65(4):515-20. DOI: http://doi.org/10.3109/09637486.2014.880671

28. Arzati MM, Honarvar NM, Saedisomeolia A, Anvari S, Effatpanah M, Arzati RM *et al*. The effects of ginger on fasting blood sugar, hemoglobin a1c, and lipid profiles in patients with type 2 diabetes. Int J Endocrinol Metab [internet]. 2017; 15(4):e57972. DOI: http://doi.org/10.5812/ijem.57927

29. Miranda Neto MV, Rewa T, Leonello VM, Oliveira MAC. Advanced practice nursing: A possibility for Primary Health Care?. Rev Bras Enferm [internet]. 2018; 71(supl 1):716-21. [Issue Edition: Contributions and challenges of practices in collective health nursing]. DOI: http://dx.doi.org/10.1590/0034-7167-2017-0672

30. Cassiani SHB, Lira Neto JCG. Nursing perspectives and the "Nursing Now" campaign. Rev Bras Enferm [internet]. 2018; 71(5):2351-2. DOI: http://dx.doi.org/10.1590/0034-7167.2018710501