DOI:10.9756/INTJECSE/V14I6.128 ISSN: 1308-5581 Vol 14, Issue 06 2022

Evaluation of the effects of synbiotic supplementation (lactobacillus acidufilus and Cinnamomum) on inflammatory condition and lipid profile in patients with type 2 diabetes

Running title: effects of Cinnamomumon on lipid profile

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Abstract

Introduction: Patients with type 2 diabetes are more likely to have cardiovascular disease (DMT2). This research was created to look into the impact of probiotics and cinnamon on lipid profiles and inflammatory markers in type 2 diabetes patients. Probiotics and cinnamon have been shown to reduce inflammation and modulate the lipid profile.

Methods: 120 DMT2 patients who were referred to the diabetic clinic in Karaj were randomly allocated to one of four groups in this crossover, double-blind, randomized clinical experiment. For three months, patients in groups 1 and 2 got one probiotic and one cinnamon capsule each, whereas those in groups 3 and 4 received one probiotic and one rice powder (placebo) capsule. At the conclusion of the intervention, lipid profile and inflammatory indicators were assessed.For statistical analysis, SPSS software used one-way variance and Tukey Analysis.

Results: Tumor necrosis factor alpha (TNF), C- reactive protein (CRP), probiotic, and synbiotic levels in the Cholesterol group are significantly lower than those in the control group (p< 0/05). Cinnamon, probiotics, and synbiotics have significantly increased in High Density Lipoprotein (HDL). LDL levels in the probiotic and cinnamon groups had significantly decreased (p< 0/05).

Conclusion: The consumption of synbiotic enhanced thelipid profile and some inflammatory biomarkers in patients with DMT2.

Keywords: DMT2, Lactobacillus, Cinnamon, Inflammatory factor, Lipid profile

Introduction

The treatment of diabetes and its associated consequences continues to be a serious problem worldwide (1). Cardiovascular problems are quite common in people with diabetes. Persons with diabetes have a 2 to 8 time's greater prevalence of death from cardiovascular illnesses than people without diabetes (2). Impaired insulin secretion, environmental insulin resistance, and increased hepatic glucose synthesis are three pathophysiological disorders that define DMT2 (3). Plasma insulin levels rise as a result of insulin resistance in diabetes, which ultimately causes blood glucose levels to rise as a result of a malfunction in the metabolism of glucose. Plasma levels of total cholesterol, very low density lipids (VLDL), and low density lipids (LDL) rise while HDL levels fall.

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An increase in triglyceride levels and a reduction in HDL cholesterol are the most typical symptoms of dyslipidemia in people with type 2 diabetes (4). The concentration of advanced glycosylation products is increased by glucose, a substance that promotes inflammation (5). By increasing oxidative stress, these products raise levels of inflammatory mediators such C-reactive protein (CRP), tumor necrosis factor alpha (TNF), and interleukin 10 (IL-10) (6). According to studies, lowering the proportion of gram-positive to gram-negative bacteria raises the production of pro-inflammatory chemicals, which in turn causes systemic inflammation (7, 8). Probiotic therapy lowers the number of gram-negative bacteria in the stomach and controls the inflammatory reaction. Probiotics are regarded as valuable diet because they are non-pathogenic bacteria that, when taken in appropriate quantities and while alive, have positive effects on the health of their hosts by restoring the balance of microbes in the gut. Probiotics are lactic acid-producing bacteria, particularly Lactobacillus acidophilus, which are often found in the gastrointestinal environment (7). Studies on probiotics and diabetes in both humans and animals have shown that they have positive effects on lowering fasting blood sugar and hemoglobin A1c, decreasing inflammatory variables, raising antioxidant levels, and boosting fat metabolism (9). By decongesting bile, hydrolyzing bile salts, and boosting cholesterol intake, these advantageous microorganisms treat lipoprotein abnormalities. By competing for resources, creating bacteriocin, and manufacturing short-chain fatty acids as a consequence of decreasing the pH of the colon, probiotics also suppress the development of gram-negative bacteria, which prevents inflammation (10). The treatment of DMT2 using herbal medicines has been done globally despite the limitations and potential side effects of conventional anti-hyperglycemic medications (1). Cinnamon is regarded as one of the most efficient medicinal herbs (11). Up to 20 times more insulin is produced when the cinnamon extract is used. In mouse adipocytes, the polyphenols in cinnamon double the rate of glucose metabolism (10). It has been shown that cinnamon extract inhibits TNF and cyclooxygenase 2, preventing the synthesis of prostaglandin E. By blocking the enzyme that produces nitric oxide, cinnamon extract reduces inflammation and may have anti-inflammatory properties (12). Arachidonic acid metabolism is inhibited by cinnamon terpene molecules. The glycosylated end products in the serum are prevented by the polyphenols in this plant (12, 13). Cinnamon usage improves insulin function in diabetics, according to different research (14). Additionally, it has been shown that consuming 1, 3, and 6 grams of cinnamon daily for 40 days has a beneficial impact on cholesterol, triglyceride, and glucose levels. We decide to research the effects of cinnamon consumption and probiotic bacteria (Lactobacillus acidophilus) on the lipid profile and inflammatory factor of DMT2 patients after considering the effects of both cinnamon and probiotic bacteria (Lactobacillus acidophilus) on patients with DMT2. A previously published research with the same criteria served as the basis for the present experiment, which was done to supplement and extend it (15).

Resources and techniques

Materials and methods

Protocol

The current study was a double-blind clinical trial, and neither statisticians nor patients knew what type of drug was being administered or how the groups were divided. The Medicinal Botanical Institute in Karaj, Iran has arranged capsules for probiotics, symbiosis, cinnamon and placebo. Lactobacillus acidophilus PTCC 1643 was obtained for use in probiotic treatment (Zist-yar Sina Co, Iran). Cinnamomumzeylanicum, a member of the family Lauraceae and the genus Camphor tree, was proposed by herbal experts. In this experiment, rice flour was used as a control substance. Placebo (0.5 g rice flour powder in solid gelatin capsules), Synbiotics (Lactobacillusacidophilus 108CFU in combination with 0.5 g cinnamon powder in solid gelatin capsules), Probiotics (Lactobacillusacidophilus108CFU in solid gelatin capsules) and cinnamon. The group was administered in sequence (0.5 g cinnamon powder in solid gelatin capsules). The 136 inclusion-based participants in this study were randomly assigned to four groups: probiotics, symbiotics, cinnamon, and controls. A grouping system by age and gender was used. The sample size was calculated to be sufficient to detect a 20 mg / dL difference in fasting blood glucose levels between groups using type I error = 0.05 and performance assumptions of 80% (15).). The patient recruitment CONSORT diagram works with the diagram. 1. We used a computer-generated random number table and block randomization using serial number bins representing blocks of 4 patients to determine how to distribute the treatment. In addition to the patient's standard medical care, the following diets were used: Group A received one Lactobacillus acidophilus 108cfu capsule and 0.5 g of cinnamon powder daily, while Group B received only one Lactobacillus acidophilus 108cfu capsule. Each day, Group C received 1 capsule containing 0.5 g of cinnamon powder and Group D received 1 capsule containing 0.5 g of rice flour powder.The conduct of the study and the possible results of dietary supplements were first explained in detail to the patient. All participants were informed that they could stop participating in the study at any time by filling out a permit and notifying their doctor of their choice. For three months, patients were instructed to take medication daily with meals and report side effects associated with the use of dietary supplements.Until it was employed in biochemical assays, serum was stored at -70°C. The trial was registered in the Iranian Clinical Trials Registry (IRCT20170305032883N2), and the ethics committee of the Alborz University of Medical Sciences in Alborz Province, Iran, approved the protocol (IR.ABZUMS.REC.1394.92).

Participants

Participants were DMT2 patients aged 40-60 years with no previous insulin use, fasting blood glucose levels of 125-250 mg / dl and HbA1c levels of 7-8%. The exclusion criteria for this study are: History of lactose intolerance or hypersensitivity. Pregnancy; Care; Use of certain medications (affects blood sugar levels such as diuretics, corticosteroids, antibiotics); Use of vitamins and medicinal plants; Changes in anti-diabetes medications over the last 4 months. Smoking and drinking(figure 1). The study did not include those who strictly followed the diet or who actively exercised. Patients had to bring a prescription to each appointment so that they could measure the consumption of different medications according to the plan. In addition, between visits, a phone call was sent to inquire about the use of the medicine. Participants were also forbidden to change their activities or diet while participating in the study.

Statistical analysis

The sample size was determined with 80% power using a two-sided test with a 5% significance level based on an effect size of 0.5 (0.5% reduction in HbA1c) (15). The sorted block randomization strategy was layered and executed by gender using an online sealed envelope application with a block size of 4 (AABB, ABAB, ABBA, BAAB, BABA, BBAA). .. Researchers, participants, and data analysts were not informed about the treatment. For statistical analysis of the data, we used version 24.0 of the Social Science Statistics Program from SPSS Inc. (Chicago, Illinois, USA). Quantitative statistics are reported using the mean standard deviation. Differences between groups after the intervention are assessed using the paired t-test. Differences between each group and control group are examined using one-way ANOVA and post-Tukey's test. A p-value less than 0.05 is a threshold for statistical significance.

Results

In this research, Table 1 summarizes the demographic data of the participants. Tables 2 and 3 describe the means of the test results at the start and conclusion of the study as well as the variations between each group and the control group.Comparing the cinnamon and synbiotic groups to the control group, LDL was dramatically reduced. In comparison to the control group, HDL levels dramatically rose in the cinnamon and synbiotic groups. When compared to the control group, the cinnamon group's cholesterol dramatically fell. TG was considerably lowered in the cinnamon group compared to the control group. In comparison to the control group, CRP considerably reduced in the synbiotic group. In comparison to the control group, TNFαwas considerably elevated in the cinnamon and synbiotic groups. IL10 was considerably elevated in the cinnamon group compared to the control group.

Discussion

The results of the investigation showed that at the end of the trial, CRP was much lower in the synbiotic group than in the cinnamon and probiotic groups. TNF levels significantly increased in the cinnamon and synbiotic groups compared to the control group. IL10 levels were also significantly higher in the cinnamon group than in the control group. Consumption of probiotic yogurt significantly reduced blood CRP levels compared to consumption of normal yogurt, but had no impact on TNF levels, according to the study by Asemi et al (16). Probiotics (Bifidobacterium langum and Escherichia coli) were shown to be more efficient than a placebo in reducing blood CRP levels in colon cancer patients, according to Zhang and colleagues (17).Serum TNF levels did not decrease after 8 weeks of taking the probiotic (Lactobacillus casei, Lactobacillus acidophilus, and Lactobacillus salivarius), according to research by Yesibua et al (18). Fedenco and others It was also mentioned that individuals with ulcerative colitis who took a synbiotic containing Lactobacillus casei for 8 weeks had a substantial reduction in TNF (19). According to studies, lipopolysaccharides cause a signaling pathway in monocytes that activates the NF-kappa. Pro-inflammatory cytokines are consequently expressed and released. By eliminating or deactivating this nuclear factor, probiotic bacteria inhibit the generation of pro-inflammatory cytokines (20, 21). By boosting the amount of natural killer T cells, probiotics may also be help reduce systemic inflammation (22).The serum HDL levels in the cinnamon and synbiotic groups were considerably higher than those in the probiotic group, according to the findings of the current investigation on blood lipid patterns. A substantial reduction in LDL was also seen in the cinnamon and synbiotic groups, but not in the probiotic group. In contrast to the probiotic and synbiotic groups, the cinnamon group had a substantial decrease in cholesterol and triglycerides whereas the probiotic and synbiotic groups did not. The results of this research, which are consistent with those of Moroti et alstudy, showed that consuming synbiotics including Lactobacillus acidophilus and Bifidobacterium bifidum dramatically raises HDL levels while having no impact on cholesterol and triglyceride levels in people with DMT2 (22). The probiotic group's HDL levels significantly increased, according to the research by Kessling et al. and Fabian et al (23, 24). Additionally, Ejtehad et al. found that in patients with DMT2, having probiotic yogurt for 6 weeks as opposed to normal yogurt dramatically lowered cholesterol (25). Probiotics have no impact on the lipid pattern, according to certain research (26, 27). However, other studies have shown that after 8 weeks, type 2 diabetes individuals who ate synbiotic bread instead of probiotic and control had significantly reduced triglyceride, LDL, and HDL values (9, 28, 29). In DMT2 patients who consumed cinnamon, Mehrzadi et al. found a considerable reduction in CHO and LDL and a significant rise in HDL levels. Patients with higher baseline BMIs (body mass index) showed these changes substantially more clearly (1). According to the proposed mechanism, probiotic bacteria lower blood cholesterol by hydrolyzing bile salts, decongesting bile and bile salts, and increasing cholesterol reabsorption while decreasing bile reabsorption (30). Short-chain fatty acids from probiotic bacteria's fermentation also prevent cholesterol synthesis (31). Different research elements, such as study design, sample size, kind and dosage of probiotic bacteria, length of intervention, and clinical characteristics of the individuals, might have resulted in different findings regarding the impact of probiotics on inflammation levels and fat patterns in diabetes (32). Overall cinnamon intake did not significantly affect fat markers in type 1 and type 2 diabetics, according to the findings of Baker et alresearch, which is a systematic review article from five clinical studies (33). Inhibiting the activity of 3-hydroxy-3-methylglutaryl-coA lyase, cinnamon has been found in other investigations to lower fat levels in mice (31). The earlier studies also showned that cinnamon might increase UCP3 gene expression, which is essential for the metabolism of fatty acids. Oxidation of fat and carbohydrates is facilitated by UCP3 gene expression (34). The expression of UCP3 regulates energy consumption via fatty acid oxidation in brown adipose tissue and skeletal muscle (11).

Conclusion

The findings show that cinnamon eating helps DMT2 patients' lipid profiles and several inflammatory markers. Contrarily, using synbiotics results in a considerable reduction in LDL and CRP levels as well as a significant rise in HDL levels.

Acknowledgment

We would like to thank the Vice Chancellor for Research of Alborz School of Medical Sciences for their assistance in implementing the above project.

Conflicts and interest

No conflicts are declared.

Disclosure

The study was approved by the Ethics Committee (IR.ABZUMS.REC.1394.92) of the Alborz University of Medical Sciences, Alborz Province, Iran.

Informed consent was obtained from all the participants.

Approval date of Registry and the Registration No: Iranian Clinical Trials Registry (IRCT20170305032883N2).

Animal studies: N/A.

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Figure legends:

Figure 1. Consort diagram of participant