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The Effect of Ginger Capsules on the Control of Blood Sugar in Gestational Diabetes: A Triple-Blind Randomized Controlled Clinical Trial

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Abstract

Objectives: Gestational diabetes is a major prenatal problem and one of the most common complications of pregnancy throughout the world. Ginger can adjust biochemical pathways that are activated in some diseases such as diabetes by affecting insulin sensitivity. The present study was conducted to assess the effect of ginger capsules on the control of blood sugar in gestational diabetes.

Materials and Methods: The present triple-blind randomized clinical trial was conducted on 76 women with gestational diabetes attending high-risk pregnancy clinics of Alzahra and Taleghani teaching hospitals and Imam Reza hospital in Tabriz in 2016. Eligible mothers were divided into intervention and control groups using block randomization. Data were analyzed using analysis of covariance (ANCOVA) and repeated measures ANOVA, chi-square, Fisher exact, chi-square for trend, Mann-Whitney, and independent t tests.

Results: No significant difference was found between two groups in terms of personal-social details ($P>0.05$). No significant difference was observed between the 2 groups after 8 weeks of intervention in terms of fasting blood sugar ($P=0.366$). However, mean blood glucose 2 hours after meals, the dose of insulin received, and frequency of visits to the gynecologist after 8 weeks of intervention were significantly lower in the intervention group compared to control group ($P<0.05$). No significant difference was found between the 2 groups in terms of Hemoglobin A1C 8 weeks after intervention ($P=0.248$).

Conclusions: Ginger capsule was able to reduce mean blood glucose 2 hours after meals, the dose of insulin received, and frequency of visits to the gynecologist in women with gestational diabetes. This medication is likely to promote the health of mothers with gestational diabetes and their infants.

Keywords: Ginger, Blood sugar control, Gestational diabetes, Hemoglobin A1C

Introduction

Gestational diabetes is a major prenatal problem throughout the world and among the most common complications of pregnancy (1). Gestational diabetes is recognized by the rise in blood glucose that is first diagnosed during pregnancy (2), and is characterized by carbohydrate intolerance and subsequent abnormal blood sugar with varying severity. Diabetic women are at risk for preeclampsia, and their embryos are exposed to the risk of developing macrosomia and perinatal disorders (3). The prevalence of gestational diabetes varies from 1% to 14% and depends on the region, the study population, and the diagnostic criteria used (4). The prevalence of this disease has been reported to be 4.4% in no-risk women and 10% in women with at least one risk factor (1).

In societies with a higher prevalence of gestational diabetes, diabetes type II is also more commonplace, and in fact, the prevalence of gestational diabetes follows diabetes type II (5). Half of the patients with gestational diabetes would eventually develop diabetes in the coming 20 years. The risk of recurrence of gestational diabetes in the next pregnancy is 40%. The risk of developing diabetes type I is estimated to be 40% for infants with diabetic parents (6).

According to the International Association for the Study of Diabetes and Pregnancy and the American Diabetes Association, glucose tolerance test two hours after the intake of 75 g of glucose following overnight fasting is recommended as the first step in diagnosing gestational diabetes during 24 to 28 gestational weeks in women with no previous diagnosis of diabetes. According to the American Diabetes Association, gestational diabetes is diagnosed with the impairment of at least 2 of these results (fasting blood sugar [FBS] >92 mg/dL, 1 hour >180 mg/dL, 2 hours >153 mg/dL) (7).

Insulin therapy is normally recommended when fasting

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or 2 HPP plasma glucose is not persistently maintained below 95 mg/dL or 120 mg/dL respectively with a standard nutritional regimen. Nutritional regimen and nutritional counseling are specifically carried out according to height and weight, and a regimen containing an average of 30 kcal/kg/d should be provided (6). Lifestyle change including the change in food regimen is among the first measures for all women with gestational diabetes to be taken. However, 7% to 20% of women fail to control blood sugar with food regimen and exercise and will require glucose-lowering medications or insulin to control their gestational diabetes (8). Complications of insulin therapy include hypoglycemia, weight gain, lipodystrophy, edema, hypertension, insulin sensitivity and allergy, and resistance to injectable insulin (9). Because of complications of insulin and the difficulty of its injectable form, complementary and alternative medications are also used.

Complementary and alternative medications are well-accepted classes of therapy. Ginger is a plant that is widely used in Asia for reducing blood sugar (10). This plant is highly likely to be native to South-East Asia and is cultivated in tropical regions of both eastern and western hemispheres. No cases of medication interaction with ginger have been reported so far. Ginger is a fairly healthy and safe medication and its use during pregnancy or otherwise has not been prohibited (11). Using more than 250 mg of ginger 4 times a day leads to hemorrhage and miscarriage in the first half of pregnancy. The use of ginger during pregnancy has not been known to cause any teratogenic complications in the fetus. The five-minute Apgar score of all infants whose mothers had used ginger during pregnancy has been 9 or 10 (12). No side-effects have been reported for ginger, only in people prone to skin rash, and stomach ache or digestive problems may be caused by daily intake of 2-4 g (11).

Ginger has been used in traditional medicine for thousands of years in a wide range of diseases such as muscular pain, fever, sore throat, indigestion, and vomiting. Ginger contains many antioxidant compounds, including gingerols, shogaols, paradols, zingerones. These antioxidants probably increase the expression of GLUT4 protein, insulin receptors, and improve the pancreatic β cells function, and thus improve glucose tolerance. Therefore, they may be effective in the treatment of diabetes and also chronic inflammation (13) and can adjust biochemical pathways that are activated in chronic inflammations (such as diabetes) (14).

In a double-blind placebo-controlled clinical trial conducted by Mozaffari-Khosravi et al, the effect of ginger on lipid and glycemic indices was assessed in patients with type II diabetes. Daily intake of 3 g of ginger powder for 8 weeks led to reduced FBS and hemoglobin A1C and a significant increase in insulin sensitivity index compared to the start of the study (15). In a study conducted by Bordia et al in India, the intake of 4 g of ginger powder by healthy people and patients with coronary artery disease with or without type II diabetes made no significant change in the blood sugar level in any of the groups (16).

In a clinical trial conducted by Mahluji et al, daily intake of 2 g of ginger for 2 months had no effect on FBS ($P = 0.42$) or hemoglobin A1C ($P = 0.66$), but reduced serum insulin ($P = 0.001$) and insulin resistance index HOMA ($P = 0.002$) (13). In a study conducted by Arablou and Naheed in Tehran, the effect of ginger on blood sugar and lipid profile was assessed. Given the effectiveness of ginger in blood sugar and lipid control, and that it can reduce blood sugar and serum insulin, and increase insulin sensitivity and improve blood lipid profile, especially in patients with type II diabetes and because of the low number of clinical trials in this field, further studies on humans with intakes of different amounts of ginger over longer periods were recommended (17).

Given the absence of studies on the effect of ginger on blood sugar in women with gestational diabetes and the conflicting reports on the effects of ginger (17), also the safety of ginger during pregnancy reported in previous studies (12), and the need to reduce insulin therapy due to the unpleasantness of its injectable form, the need for proper training for the right injection site, and also cost-effectiveness of ginger compared to insulin for diabetic patients, and easy administration of oral medications and its acceptability by mothers (18), we decided to assess the effect of ginger on blood sugar control in women with gestational diabetes, so that the results can help reduce complications of high-risk pregnancies and promote maternal and neonatal health.

Materials and Methods

The Study Type and Participants

The present triple-blind randomized clinical trial study was conducted to assess the effect of ginger intake on gestational diabetes on 76 eligible diabetic pregnant women attending high-risk pregnancy clinics of Alzahra and Taleghani teaching hospitals and diabetic clinic of Imam Reza hospital in Tabriz in 2016.

The total sample size required was determined to be 32 women based on the results obtained in studying "The effect of probiotics on metabolic health of women with gestational diabetes" by Lindsay et al (19), taking into account $m_1 = 4.85$ nmol/L (mean FBS), assuming 10% reduction in the mean FBS due to intervention $m_2 = 4.36$ mmol/L, and $sd_1 = sd_2 = 0.58$, $\alpha = 0.05$, and Power = 0.95, which was raised to 38 women per group, taking into account 20% loss.

Inclusion Criteria

18-35-year-old mothers, with gestational age of 24 to 28 weeks and singleton pregnancy based on ultrasound, diabetic pregnant mothers receiving insulin, normal blood pressure (<140.9 mm Hg) in current pregnancy and

no proteinuria in pregnancy tests, with at least primary school education, willingness to take part, phone number and address for follow-up, health record in Alzahra and Taleghani teaching hospitals and diabetic clinic of Imam Reza hospital in Tabriz were included in the study. Exclusion criteria were: Use of alcohol or smoking, use of traditional medicine medications, especially cinnamon, a history of chronic hypertension and blood sugar <70 mg/dL.

Sampling

Sampling was conducted in Alzahra and Taleghani hospitals and diabetic clinic of Imam Reza in Tabriz, where diabetic pregnant women were assessed in terms of inclusion and exclusion criteria. The study objectives and method, and voluntary participation and ability to withdraw at any stage were fully explained to eligible women, and then, written informed consent was obtained from them. After the initial selection of the samples, FBS test, 2-hour postprandial (2hpp) blood sugar monitoring, and initial blood pressure to assess the incidence of preeclampsia, and urine test for the incidence of urinary tract infection were taken from all participants.

Randomization and Intervention

Sampling was carried out by block randomization. For complete concealment of allocations, different block sizes were used (blocks of 4 and 6). After listing nearly all the possibilities and assignment of a number to each using www.random.org, samples were selected by simple randomization by replacing blocks, so that total sample size required (76 pregnant women with diagnosed gestational diabetes) was gradually selected. Successively numbered sealed envelopes were used for allocation concealment. Envelopes were numbered from 1 to 76. After the selection of samples, obtaining their informed consent and completion of their baseline data, for sampling, envelopes were opened in order of numbers.

To prepare ginger supplements, dry ginger was purchased from a reputable herbalist, ground and then turned into 500 mg ginger rhizome capsules. Wheat flour placebo capsules were prepared in the same form, color and dosage as ginger capsules. To produce the scent of ginger in these capsules, they were kept in the vicinity of ginger powder for 2 weeks and then packed in similar boxes. Microbial and physicochemical tests were carried out on ginger, and medication and placebo were coded. All these stages were performed at School of Pharmacy, Tabriz University of medical sciences, Tabriz, Iran. Eligible mothers with gestational age of 24 to 28 weeks who had been diagnosed with gestational diabetes according to FBS and 2-hour oral glucose tolerance test (OGTT), and despite their food regimen and lack of blood sugar control (the dose of insulin required was determined by a specialist based on the individual's condition and blood sugar level) insulin therapy had been initiated for them were included in the study. Intervention and control groups respectively received 500 mg ginger capsules and 500 mg placebo capsules twice a day for 8 weeks from the 28th week of pregnancy. FBS and 2hpp tests were performed every 2 weeks. To assess fetal anthropometric parameters based on ultrasound requested by the specialist in the 36th week of pregnancy (eight weeks after intervention), ultrasound was performed by a sonographer (a project collaborator), and the results were recorded in a checklist. HbA1c test was prescribed by the specialist at the end of intervention and performed at the laboratory of Behbood hospital, Tabriz, Iran, and recorded in the checklist. The demographic details questionnaire was completed by the researcher by interviewing participants.

Data Collection Tools

In the present study, data were collected using the following tools: Demographic and midwifery questionnaire, blood sugar control checklist, insulin dosage and the number of visits to the gynecologist checklist, hemoglobin A1C checklist, and satisfaction and side-effects checklist. Participants were visited by the perinatologist in high-risk maternity clinics every 2 weeks and checklists were completed by the researcher. Validity of the above-mentioned checklists was determined through face and content validities so that checklists were made available to 8-10 faculty members of School of Nursing and Midwifery in Tabriz and after corrections, their final views were implemented. To assess the reliability of laboratory techniques, blood samples were taken from 10 pregnant mothers for the blood sugar test. These samples were examined once by the laboratory technician and then by another colleague and the correlation coefficient was 1.

Analysis of Data

Data collected from all participants were analyzed using SPSS version 21.0. Descriptive and analytical statistics were used. Normal distribution of the quantitative data was determined using the Kolmogorov–Smirnov test. The 2 groups were compared in terms of personal-social details using chi-square, chi-square for trend, Fisher exact test, and independent *t* tests. With the baseline values controlled, analysis of covariance (ANCOVA) test was used to compare the 2 groups in terms of fasting and postprandial blood sugar levels after the intervention. The two groups were compared in terms of hemoglobin A1C level and the frequency of pregnancy visits using independent *t* test, and in terms of satisfaction, using Mann-Whitney test. In all stages, $\alpha = 0.05$ was considered significant. All analyses were carried out according to "Intention to treat analysis".

Results

In the course of the study, one woman was excluded for

unwillingness to continue, and ultimately, data collected from 75 women (37 in the intervention group and 38 in control) who remained in the study until the end were analyzed. All pregnant women in both groups used injectable insulin.

Mean (standard deviation) of age was 30.7 (5.8) years in the intervention group and 32.5 (4.7) years in control. Participants' personal-social details are presented in Table 1, which shows no significant difference between the 2 groups, except in terms of parity ($P > 0.05$).

Independent t-test showed significant differences between the 2 groups before the intervention in terms of fasting and 2hpp blood sugar levels ($P = 0.024$). However, with baseline values controlled, ANCOVA test showed no significant difference between the 2 groups in terms of FBS 8 weeks after intervention ($P = 0.366$).

Independent *t* test showed no significant difference between the 2 groups before intervention in mean 2hpp blood sugar ($P = 0.181$), but with baseline values controlled, ANCOVA test showed a significant difference between them 8 weeks after intervention ($P = 0.000$).

Independent *t* test showed no significant difference between the 2 groups before intervention in mean 2hpp blood sugar ($P = 0.516$), but with baseline values controlled, ANCOVA test showed a significant difference between them 8 weeks after intervention ($P = 0.01$).

Independent *t* test showed no significant difference between the 2 groups before intervention in mean 2hpp blood sugar ($P = 0.351$), but with baseline values controlled, ANCOVA test showed a significant difference between them 8 weeks after intervention ($P = 0.000$) (Table 2).

With regards to the dose of insulin in the first month received by the study groups, independent t-test showed no significant difference between the two groups in terms of breakfast dose ($P = 0.074$), but the 2 groups were significantly different in terms of dinner dose ($P = 0.014$). Regarding the insulin dose in the second month, independent *t* test showed no significant difference between the 2 groups in terms of breakfast dose ($P = 0.11$), but the 2 groups were significantly different in terms of dinner dose of insulin ($P = 0.001$) (Table 2).

According to independent *t* test, there was no significant difference between two groups in terms of mean concentration of hemoglobin A1C ($P = 0.248$), but

Table 1. Frequency Distribution of Certain Personal-Social Details of the Study Groups

Personal-Social Details	Ginger Group (n = 38), No. (%)	Placebo Group (n = 38), No. (%)	*P*
Age (y)			0.151[b]
	30.7 (5.8)[a]	32.5 (4.7)[a]	
Gestational age			0.212[b]
	27.6 (1.2)[a]	27.2 (1.5)[a]	
BMI (kg/m^2)			
	28.0 (4.6)[a]	28.9 (4.2)[a]	
Education			0.440[c]
High school and lower	19 (50)	19 (50)	
High school/diploma	17 (44.7)	14 (36.9)	
University	2 (5.3)	5 (13.2)	
Mother's occupation			0.380[e]
Housewife	36 (94.7)	37 (97.4)	
Employed	2 (5.3)	1 (2.6)	
Number of pregnancies			0.061[e]
1	7 (18.4)	6 (15.8)	
2	16 (42.1)	23 (60.5)	
3	10 (26.3)	7 (18.4)	
4	4 (10.5)	1 (2.6)	
5	1 (2.6)	1 (2.6)	
Parity			0.0036[e]
0	7 (18.4)	7 (18.4)	
1	17 (44.7)	24 (63.2)	
2	10 (26.3)	6 (15.8)	
3	3 (7.9)	1 (2.6)	
4	1 (2.6)	0 (0.0)	
Spouse's occupation			0.636[e]
Unemployed	4 (10.5)	6 (15.8)	
Employed	0 (0.0)	0 (0.0)	
Manual worker	16 (42.1)	12 (31.6)	
Shopkeeper	5 (13.2)	8 (21.1)	
Spouse's education			0.247[c]
High school and lower	23 (60.6)	17 (44.7)	
High school/diploma	10 (26.4)	16 (42.1)	
University	5 (13.2)	5 (13.2)	
High school and lower	23 (60.6)	17 (44.7)	
Adequacy of family income			0.709[c]
Adequate	3 (7.9)		
Fairly adequate			
Inadequate	19 (50)		
Place of residence			0.691[d]
Private	20 (52.2)	24 (63.2)	
Rental	14 (36.8)	11 (28.9)	
Parents' house	3 (7.9)	4 (10.5)	
History of fetal abnormalities			0.500[d]
With	0 (0.0)	1 (2.6)	
Without	38 (100.0)	37 (97.4)	
Stillbirth			0.307[d]
With	3 (7.9)	1 (2.6)	
Without	35 (92.1)	37 (97.4)	
Preterm childbirth			0.155[d]
With	3 (7.9)	7 (18.4)	
Without	35 (92.1)	31 (81.6)	
Infertility			0.500[d]
With	2 (5.3)	3 (7.9)	
Without	36 (94.7)	35 (92.1)	
Miscarriage			0.215[d]
With	2 (5.3)	5 (13.2)	
Without	36 (94.7)	33 (86.8)	
Type of pregnancy			0.632[d]
Wanted	33 (86.8)	33 (86.8)	
Unwanted	5 (13.2)	5 (13.2)	

[a] Mean (SD); [b] Independent *t* test; [c] Chi-square for trend; [d] Fisher exact test; [e] Chi-square test.

Table 2. Comparison of FBS, 2hpp, and Dose of Insulin Before and After Intervention in Intervention and Control Groups

Variable	Ginger Group n = 37 Mean (SD)	Placebo Ggroup n = 38 Mean (SD)	Comparing Ginger and Placebo Groups AMD (95% CI)	*P* Value
FBS				
Before intervention	97.0 (7.5)[a]	101.3 (8.6)[a]	-4.34 (-8.10 to-0.57)	0.024[a]
2 weeks after intervention	93.7 (6.0)	93.1 (5.1)		
4 weeks after intervention	90.8 (7.5)	92.9 (4.6)	-0.84 (-2.71 to1.01)	0.366[d]
6 weeks after intervention	89.1 (6.6)	92.3 (4.7)	0.141[b]	
8 weeks after intervention	86.8 (7.1)	88.5 (6.7)	0.352[c]	
Blood sugar 2 hours after breakfast				
Before intervention	144.4 (12.0)[a]	148 (10.5)[a]	-3.62 (-8.97 to 1.72)	0.181[a]
2 weeks after intervention	131.5 (9.2)	135.3 (8.3)		
4 weeks after intervention	131.0 (5.7)	133.9 (6.5)	-5.05 (-7.61 to -2.48)	0.181[a]
6 weeks after intervention	122.8 (7.9)	129.0 (8.6)	0.000[b]	
8 weeks after intervention	118.6 (7.5)	125.8 (7.4)	0.404[c]	
Blood sugar 2 hours after lunch				
Before intervention	146.2 (8.4)[a]	144.8 (9.1)[a]	1.37 (-2.81 to 5.5)	0.516[a]
2 weeks after intervention	133.1 (5.1)	133.7 (6.4)		
4 weeks after intervention	127.9 (8.1)	133.8 (9/6)	-2.99 (-5.25 to 0.73)	0.010[d]
6 weeks after intervention	123.0 (5.9)	127.3 (8.0)	0.000[b]	
8 weeks after intervention	118.5 (6.0)	122.8 (6.7)	0.468[c]	
Blood sugar 2 hours after dinner				
Before intervention	140.4 (6.9)[a]	142.3 (10.2)[a]	-1.96 (-6.12 to 2.20)	0.351[a]
2 weeks after intervention	129.3 (7.4)	134.5 (8.0)		
4 weeks after intervention	124.5 (9.2)	132/9 (10.1)	-5.96 (-9.08 to -2.90)	
6 weeks after intervention	121.8 (6.9)	128.7 (10.7)	0.000[b]	
8 weeks after intervention	120.1 (7.2)	123.6 ()6.4	0.383[c]	
Dose of insulin (1st month)				
Breakfast	148.4 (18.8)[a]	156.4 (19.2)	-7.96 (-16.71 to 0.793)	0.074[a]
Dinner	145.0 (16.9)[a]	155.6 (19.2)[a]	-7.83 (-18.91 to -2.18)	0.014[a]
Dose of insulin (2nd month)				
Breakfast	150.4 ()16.9[a]	158.2 (24.2)[a]	-10.55 (-17.48 to 1.82)	0.110[a]
Dinner	143.2 (16.4)[a]	158.1 (19.8)[a]	-14.83 (-23.23to -6.43)	0.001[a]

Abbreviations: 2hpp, 2-hour postprandial; FBS, fasting blood sugar; AMD, adjusted mean difference.
[a] Independent *t* test.
[b] Interactive effect of time on intervention.
[c] Interactive effect of group on intervention.
[d] Repeated measures ANOVA, with baseline values controlled.

Table 3. Number of Visits and Mean Hemoglobin A1C in the Study Groups

Variable	Ginger Group (n = 37) No. (%)	Placebo Group (n = 38) No. (%)	*P* Value
Number of visits to gynecologist	0.60(0.0-2.0)	1.39(0.0-3.0)	0.000[a]
Hemoglobin A1C	6.1(0.49)	6.2(0.52)	0.248[a]

[a] Independent *t* test.

this test showed a significant difference between them in terms of visits to the gynecologist ($P < 0.001$) (Table 3).

Twenty-three women (60.5%) from the intervention group and 16 from control (42.1%) were satisfied with the medication used, and Mann-Whitney test showed no significant difference between the 2 groups in terms of satisfaction with medication ($P = 0.332$) (Table 4).

The medication side-effects were reported as follows: Vaginal hemorrhage: very low and equal in both groups (3 [7.9] women); Lower abdominal pain: very low in intervention group (1 [2.6] women); Backache: very low in intervention group (2 [5.3]) and low in control (1 [2.6]); Skin rash: very low in intervention (5 [13.2]) and in control (3 [79]) groups, low in intervention group (2 [5.3]) and moderate in intervention group (2 [5.3]); Flatulence: very low (1 [2.6]) and low (1 [2.6]) in control group, and very high (1 [2.6]) in intervention group; Dizziness: very low and equal in both groups (4 [10.5]), low (3 [7.9]) in intervention group, and (2 [5.3]) in control (Table 5).

Discussion

The present study was the first in the world to have

Table 4. Mothers' Satisfaction with Medication Received in the Study Groups

Variable	Ginger Group (n = 37) No. (%)	Placebo Group (n = 38) No. (%)	*P* Value
Mothers' satisfaction with medication received			0.332[a]
Vary satisfied	6 (15.8)	8 (21.1)	
Satisfied	23 (60.5)	16 (42.1)	
Equally satisfied and dissatisfied	7 (18.4)	11 (28.9)	
Dissatisfied	1 (2.6)	2 (7.9)	
Very dissatisfied	0 (0.0)	0 (0.0)	

[a] Mann-Whitney test.

addressed the effect of ginger on gestational diabetes and showed that daily intake of 1-g ginger capsules for 8 weeks by patients with gestational diabetes controlled 2hpp blood sugar, reduced dose of insulin received and the number of visits to the gynecologist in diabetic pregnant mothers.

In a double-blind randomized clinical trial conducted by Mahluji et al on sixty-four 38-65-year-old diabetics, the anti-inflammatory effect of ginger capsules on diabetes type II was assessed in Tabriz. It was observed that daily intake of 2 g of ginger for 2 months had no effect on FBS or hemoglobin A1C, but reduced serum insulin, insulin resistance index, and chronic complications relating to diabetes type II (13). These results agree with those found in the present study regarding the fact that ginger capsules were unable to reduce FBS and hemoglobin A1C.

In a study conducted in India by Bordia et al, 4 g of ginger powder was given to healthy people and patients with coronary artery disease with or without diabetes type II. However, no significant change was observed in blood sugar in any of the groups (16). These results agree with those found in the present study regarding the fact that ginger capsules were unable to reduce FBS.

Talaei et al conducted a double-blind randomized controlled clinical trial in 2012 in which the effect of ginger on blood sugar and lipid indices in 87 patients with diabetes type II was examined in Yazd. Data obtained from 81 patients who stayed in the study for 8 weeks were analyzed. All patients used oral glycemic control drugs. The results obtained showed that ginger capsules were beneficial to these diabetic patients, since they reduced LDL-C, FBS, and glycosylated hemoglobin A1C, and increased apolipoprotein A1 (20). These results disagree with those of the present study, probably because of the type of disease or participants, which requires further research.

A double-blind randomized controlled clinical trial was conducted by Arablou et al to determine the effect of ginger supplements on certain risk factors for cardiovascular diseases in patients with diabetes type II who were randomly assigned to ginger and placebo groups. The intervention lasted for 12 weeks. The data obtained from 64 patients were analyzed and it was shown that the intake of ginger significantly reduced FBS, triglyceride, total serum cholesterol, and C-reactive protein (CRP) in the intervention group compared to control ($P<0.05$). Changes in cholesterol low-density lipoprotein (LDL), high-density lipoprotein (HDL), systolic and diastolic blood pressures and waist circumference were not significant ($P>0.05$). Their study showed that the intake of ginger reduces certain cardiovascular risk factors such as FBS, triglyceride, serum total cholesterol, and CRP in patients with diabetes type II, and can reduce the development of cardiovascular diseases in these patients. Although their results failed to show the effect of ginger on serum HDL and LDL, or systolic and diastolic blood pressures and waist circumference (21), they disagree with the present study results in terms of reduced FBS, which may have been due to the effects of nutrition regimen and medications used by these patients. Moreover, the study subjects, type of disease, and duration of intervention were different from those in the present study.

According to a study conducted by WHO entitled "Ginger" (*Zingiber officinale* Roscoe) in 1999, no medication interaction with ginger has been reported so far. Ginger is a fairly healthy and safe medication and its use during pregnancy or otherwise has not been prohibited. Using more than 250 mg of ginger 4 times a day leads to hemorrhage and miscarriage in the first half of pregnancy. No side-effects have been reported for ginger, except for the skin rash in people prone to it (11). These results agree with the results of the present study in terms of side-effects.

The results of a study conducted by Narenji et al to compare the effects of powder and fresh roots of ginger on pregnancy nausea and vomiting in Arak showed a high level of mothers' satisfaction with this medication, and none of them was unhappy with this medication, and no side-effects were reported (22). These results agree with those of the present study in terms of side-effects and patient satisfaction. Concerning 2hpp and comparison of the number of visits to the gynecologist, no clinical trial was found in the search conducted in databases.

The strong points in the present study included total blinding (no bias in participation, measurement, or results), objectivity of results, over 80% satisfaction, no reports of serious side-effects, and a high percentage of acceptance of capsules by patients. The study limitations

Table 5. Frequency of Side Effects of Medication Used in the Study Groups

Variable	Ginger group (n=37) No. (%)	Placebo group (n=38) No. (%)
Vaginal hemorrhage		
Very low	3(7.9)	3 (7.9)
Low	0 (0.0)	1 (2.6)
Moderate	0 (0.0)	0 (0.0)
High	0 (0.0)	0 (0.0)
Very high	0 (0.0)	0 (0.0)
Lower abdominal pain		
Very low	0 (0.0)	0 (0.0)
Low	1 (2.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
High	0 (0.0)	0 (0.0)
Very high	0 (0.0)	0 (0.0)
Backache		
Very low	2 (5.3)	0 (0.0)
Low	0 (0.0)	1 (2.6)
Moderate	1 (2.6)	1 (2.6)
High	0 (0.0)	0 (0.0)
Very high	0 (0.0)	0 (0.0)
Skin rash		
Very low	5 (13.2)	3 (7.9)
Low	2 (5.3)	1 (2.6)
Frequency of side-effects		
Moderate	2 (5.3)	1 (2.6)
High	0 (0.0)	0 (0.0)
Very high	0 (0.0)	0 (0.0)
Flatulence		
Very low	0 (0.0)	1 (2.6)
Low	0 (0.0)	1 (2.6)
Moderate	0 (0.0)	0 (0.0)
High	0 (0.0)	0 (0.0)
Very high	1 (2.6)	0 (0.0)
Dizziness		
Very low	4 (10.5)	4 (10.5)
Low	3 (7.9)	2 (5.3)
Moderate	1 (2.6)	0 (0.0)
High	0 (0.0)	0 (0.0)
Very high	0 (0.0)	0 (0.0)
Stomach ache		
Very low	5 (13.2)	6 (15.8)
Low	4 (10.5)	1 (2.6)
Moderate	2 (5.3)	0 (0.0)
High	0 (0.0)	0 (0.0)
Very high	0 (0.0)	0 (0.0)

included apprehensiveness of mothers about side-effects and their lack of knowledge and desire to use this medication, which required more education and guidance, and therefore the researcher spent more time counseling mothers.

Suggestions for Further Studies

Given that no side-effects have been reported for use of ginger in humans, measurement of greater number of diabetes risk factors such as triglyceride, cholesterol, LDL, and HDL tests is suggested Regarding the low number of clinical trials in this field, conducting greater number of human studies with different amounts of ginger over longer periods, prevention of gestational diabetes according to new criteria, long-term maternal and neonatal complications of gestational diabetes, and the effect of appropriate treatment on long-term maternal and neonatal outcomes are recommended.

Conclusions

The results of the present study showed that ginger capsules were able to reduce mean 2hpp and the dose of insulin received, as well as the number of visits to the gynecologist in women with gestational diabetes. Thus, given the prevalence of gestational diabetes, blood sugar level can be reduced and gestational diabetes can be somewhat controlled with this medication. Moreover, this plant can be easily used as an inexpensive and cost-effective substance during pregnancy to promote maternal and neonatal health.

Conflict of Interests

Authors have no conflict of interests.

Ethical Issues

The present study was approved by the Ethics Committee of Tabriz University of Medical Sciences (Code: IR.TBZMED.REC.1395, 103) and registered in the Iranian Registry of Clinical Trials (No: IRCT20160404327N36). .

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