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Research Article

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The Effects of Standardized Extract of Ginseng (G115) on Blood Sugar Control and Inflammatory Factors in Patients with Type 2 Diabetes: A Double-Blind Clinical Trial

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ABSTRACT

Ginseng has been used as a treatment for different diseases in East Asian countries for many years. Most studies have examined its anti-diabetic effects in animals, but the results of a few studies done on human are controversial. This double blind clinical trial was performed on 40 patients with type 2 diabetes (20 in the intervention group and 20 in the control group) in Ahvaz Countyin 2012. The intervention group received three 100 mg capsules of standardized ginseng extract daily and the control group received placebo. After eight weeks, anthropometric indices and glycosylated hemoglobin (HbA1c), fasting blood sugar (FBS), interleukin 6 (IL6), tumor necrosis factor (TNFα), and high sensitive C- Reactive Protein (hsCRP) were studied. No significant differences were observed in anthropometric indices, glycated hemoglobin, and TNFαin the case and control groups before and after intervention. At the end of the study, a significant reduction was observed in FBS, IL6($P<0.05$) and hsCRP ($P<0.001$) in the treatment group. Furthermore, the intervention and control groups were significantly different in FBS, IL6 and hsCRP at the end ofthe study ($P<0.05$).Eight-week administration of standardized ginseng extract reduced FBS, IL6 and hsCRP in patients with type 2 diabetes. This study has been registered at the Iranian Registry of Clinical Trials (IRCT registration number: IRCT2013040812949N1).

Keywords: Ginseng, Diabetes, Glycated Hemoglobin, Blood Glucose, Inflammatory Factors

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INTRODUCTION

Diabetes is known as the most common metabolic disease around the world and about 1700 people are added to the population with diabetes, daily; meanwhile, about 85-90% of people diagnosed with diabetes are patients with type 2 diabetes (1).Prevalence of type 2 diabetes in 2000 has been reported to be about 171 million (or 2.8%) and it is predicted that this figure will become twice in 2030 (2). According to the Center for Diabetes in Iran, about 2.5 million people suffer from with type-2 diabetes (3). Type 2 diabetes is considered as one of the most important

factors in creating and exacerbating cardiovascular diseases. Dyslipidemia in patients with diabetes, including risk factors, is effective in this subject; but, a pre-inflammatory state is observed in patients with diabetes which can be involved in macro vascular complications.

During recent years non-medication based techniques have been dramatically developed for the treatment of different disorders including physical agents and herbal agents. Since inflammatory markers can be predictive of vascular injury, including atherosclerosis (4), remedial measures to reduce inflammatory cytokines can protect people from cardiovascular damage. Meanwhile, for many years, the root of the Panax ginseng (Asian or Korean Red Ginseng) has been used as a medicinal plant in East Asian countries and so far, 200 effective substances have been extracted from Panax ginseng of which ginsenonids, and polyacetylenes, alkaloids, polysaccharides, oligosaccharides, oligopeptides, flavonoids, lipids, vitamins and minerals can be mentioned(5).Previous studies have shown that Ginsenonids and their metabolites are primarily responsible for the therapeutic effects of ginseng extracts(6). Most of the conducted studies have focused on anti-inflammatory effects of ginseng on laboratory animals or in vitro(7), (8). According to the survey conducted it appears that studies on humans have not examined a long-term effect of ginseng (as a standardized extract) on the profile of inflammatory factors in patients with type 2 diabetes. Therefore, the purpose of this study was to determine the effect of standardized extract of ginseng on glycemic profile and inflammatory factors in patients with type 2 diabetes.

MATERIALS AND METHODS

The double-blind clinical trial study was performed on patients with non-insulin dependent diabetes in the diabetes clinic of Golestan Hospital in 2012. This study was approved by the ethics committee of the vice chancellor deputy at Ahvaz Jundishapur University of Medical Sciences. 60 people were selected according to an inclusion and exclusion criteria, and medical records. The inclusion criteria were: 1) diabetes type-2 for two years; 2) and aged between 30 to 60 years. Exclusion criteria included diseases of kidney, liver, parathyroid, and gastrointestinal inflammatory diseases, pregnancy and lactation, the use of insulin and nonsteroidal anti-inflammatory drugs, people with a BMI more than 35 kg/m^2 and those who had followed a weight loss diet.

To participate in the study, after the interview and explanation of the objectives of the work, 40 people expressed their satisfaction. The subjects were randomly divided into two groups - the intervention group (20 patients) and the control group (20 patients) - and they were investigated for 60 days. Patients in the intervention group received a daily dose of 300 mg standardized ginseng extract (three capsules per day taken with food consumption) for 8 weeks.

Moreover, the control group received three similar capsules as placebo. The doctor was asked to not change the types and doses of medications in order to make the drug investigation possible. Anthropometric indicators including height, weight, BMI (Body Mass Index), and WHR (waist-to-hip ratio) were measured at the beginning and at the end of the study. The venous blood samples were taken at the beginning and also at the end of the study, and fasting blood glucose, HbA1c, IL6, TNFα, and hsCRP were measured by an expert according to standard methods. Glycated hemoglobin levels (Nycocard Kit, Norway), IL6, TNFα (orgenium Kit, Finland) and hsCRP (LDN kit, Germany) were measured by ELISA. All data were expressed as mean ± SD.

RESULTS

The study was performed on40 patients (20 patients receiving standardized extract of ginseng, including 14 women and 6 men, 20 controls, including 14 women and 6 men). At the baseline, the two studied groups had no significant difference in terms of anthropometric and biochemical indices (Table 1). Analysis of nutrient intake in the case and control groups before and after intervention showed no meaningful difference. Types and doses of medications during the study remained unchanged. After eight weeks of intervention using a standardized extract of ginseng, no significant difference was observed between the groups in anthropometric parameters, including weight, BMI and WHR(Table 2).Comparing the concentration of fasting blood glucose as well as serum IL6 ($p<0.05$) and hsCRP($p<0.001$) in the case group after intervention with that prior to intervention showed a major decrease (Table 2).

Also, percentages of Hb A_1C and TNFα showed a minor decrease, which means that they were not statistically significant. During the study, statistically significant changes were not observed in biochemical parameters in the

control group (Table 2). In addition, the mean change in biochemical parameters before and after intervention between the two groups showed significant differences in fasting blood glucose levels, IL6 and hsCRP in the group taking a standardized extract of ginseng compared to the control group (Table 3).

Table 1. Basic characteristics of study subjects (values are expressed as mean ± SD)

Anthropometric index	Ginseng group (n = 20)	Placebo group (n = 20)	Pvalue
Age (year)	47.9±4.7	47.3±6.4	0.71
Weight (kg)	74.75±10.49	72.25±14.98	0.54
BMI (kg/m^2)*	29.29±3.61	27.19±4.71	0.12
WHR**	0.89± 0.12	0.88±0.12	0.89
FBS (mg/dl)	147.70±12.35	141.55±14.51	0.15
HbA1C (%)	7.43±1.42	7.82±1.44	0.40
IL6 (pg/ml)	8.43±1.17	8.17±1.22	0.60
TNFα (pg/ml)	39.13±10.8	42.93±14.32	0.34
hsCRP (mg/l)	3.61±0.49	3.55±0.36	0.69

* *Body mass index*
** *Waist: hip ratio*

Table 2. Between treatment differences in anthropometric and biochemical indices following 8-week supplementation with Ginseng or placebo in subjects with T2D (values are expressed as mean ± SD (a) significant difference compared to baseline (p<0.05) (b) significant difference compared to baseline (p<0.001))

Anthropometric index	Treatment (n = 20)			Pelacebo (n = 20)		
	Baseline	**8-weeks**	**P value**	**Baseline**	**8-weeks**	**P value**
Weight (kg)	74.75±10.49	74.55±10.53	0.57	72.25±14.98	71.95±15.13	0.36
BMI (kg/m^2)	29.29±3.61	29.14±3.74	0.31	27.19±4.71	27.07±4.59	0.36
WHR	0.89± 0.12	0.88±0.11	0.60	0.88±0.12	0.88±0.12	0.29
FBS (mg/dl)	147.70±12.35	132±16.34	<0.05	141.55±14.51	144.15±10.54	0.40
HbA1C (%)	7.43±1.42	7.28±1.09	0.40	7.82±1.44	7.87±1.43	0.52
IL6 (pg/ml)	8.43±1.17	6.79±1.39	<0.05	8.17±1.22	7.85±.69	0.16
TNFα (pg/ml)	39.13±10.8	35.66±8.08	0. 22	42.93±14.32	39.4±9.66	0.24
hsCRP (mg/l)	3.61±0.49	3.03±0.33	<0.001	3.55±0.36	3.49±0.39	0.66

Table 3. Mean difference (treatment versus placebo) (Values are expressed as mean ± SD)

Anthropometric index	Treatment (n = 20)	Placebo (n = 20)	P value
Weight (kg)	0.2±1.57	0.3±1.45	0.83
BMI (kg/m^2)	0.14±0.63	0.11±0.56	0.87
WHR	0.002± 0.01	0.004±0.01	0.65
FBS (mg/dl)	15.7±21.54	-2.6±13.63	<0.05
HbA1C (%)	0.15±0.81	-0.05±0.34	0.3
IL6 (pg/ml)	1.64±1.79	0.32±0.98	<0.05*
TNFα (pg/ml)	3.47±12.45	3.53±13.1	0.98
hsCRP (mg/l)	0.57±0.51	0.06±0.62	<0.05*

* *Significant difference between therapies (P<0.05)*

DISCUSSION

This study showed that eight weeks of intervention using a standardized extract of ginseng can reduce IL6 and hsCRP in patients with type II diabetes. Since long ago, the root of the Panax ginseng (Asian or Korean) has been used as a health booster. Various in vitro and in vivo studies have shown that ginseng extracts modulate immune responses. It seems that ginseng extract causes an increase in the host resistance by stimulating the immune system (9). Moreover, the effect of ginseng on macrophages results in the production of inflammatory cytokines such as TNFα, IL-1β, IL-6 and IFNs (10). On the other hand, it is proposed that ginseng saponins inhibit stress in rats by inhibiting the production of IL-6 (10). Chang's study examined the effect of Korean red ginseng extract on human skin cells with eczema. The results showed that ginseng extract reduces the production of TNFα and IL8 in these cells (11). Also, Zhu and coworkers in an in vitro study in China showed that Rb1 Ginsenonids, an ingredient of ginseng, lower the expression and value of TNFα and IL6 levels (12). But, the present study's results suggest that TNFα does not change. Nonetheless, as assessed by similar studies, the IL6 and hsCRP levels in type II diabetic patients who used a standardized extract of ginseng for eight weeks showed a considerable decrease compared to the control group. Dose, duration and method of operation could be the reason for the observed different results between various studies.

In the current study, treatment with ginseng extract caused a significant drop in fasting glucose. But the reduction in glycosylated hemoglobin was not appreciable. The results of the present study are consistent with those presented by Vuksan and coworkers (13).

Our results also demonstrated that 6 grams per day of Korean red ginseng for 12 weeks improved blood sugar levels, insulin plasma levels. Nevertheless, it does not have any sensible impact on the amount of glycated hemoglobin in patients with type 2 diabetes (13). The results are inconsistent with those reported by Klein and colleagues (14). Their results showed that the intervention of ginseng (8 g/day) and ginsenonids Re (250-500 mg/day) in obese people with diabetes had almost no effect in the control of blood sugar or HbA1C after 30 days (14). Furthermore, Jonathon and colleagues showed that 200 mg of ginseng extract in healthy subjects did not produce significant differences in blood glucose or HbA1C status in the intervention group as compared to the control group (15). Our current results are different from these outcomes in terms of the effects of ginseng on glucose. The difference in results may be due to the study of different target groups. The former study examined healthy subjects while the present one has examined patients with diabetes.

The results of this study provide evidences that show a ginseng extract can reduce blood sugar in people with diabetes and inflammatory factors and may be recommended to prevent long term complications associated with diabetes

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