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Original article

Effects of dried licorice extract with low-calorie diet on lipid profile and atherogenic indices in overweight and obese subjects: A randomized controlled clinical trial

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Abstract

Introduction: Licorice root is one of the most frequently used medicinal herbs. There is contradictory evidence about effects of the licorice on lipid profile. The aim of the present study was to compare effects of licorice extract concurrent with low-calorie diet with low calorie diet alone on the lipid profile and atherogenic indices in overweight and obese subjects.

Methods: In this double blind randomized controlled clinical trial, 64 overweight and obese subjects, aged 30–60 years old, were recruited from March to September 2013. They were randomly divided into intervention ($n = 32$) and control ($n = 32$) groups. Participants and research staff were masked to the treatment allocation by randomization. Both the groups received 1.5 g/day of dried licorice extract or placebo, respectively, concurrent with weight loss diet for 8 weeks. Lipid profile, weight and dietary intake were measured at baseline and at the end of the study. Body mass index and atherogenic indices were calculated.

Results: Fifty-eight participants completed the trial. At baseline, there were no significant differences for lipid profile except for low density lipoprotein-cholesterol (LDL-c) level between the groups. After the intervention, total cholesterol (TC), LDL-c levels, TC/high-density lipoprotein (HDL-c), LDL-c/HDL-c ratios and log of TG/HDL-c were significantly decreased ($p < 0.01$ for all variables), but no changes were observed in TG and HDL-c levels.

Conclusions: It seems that supplementation with licorice extract used concurrently with a low calorie diet can efficiently improve the lipid profile in overweight and obese subjects.

Keywords: Licorice; Lipid profile; Atherogenic status; Obesity; Weight loss

Introduction

Cardiovascular disease (CVD) is an important public health concern in both developed and developing countries. A major risk factor for developing the CVD is dyslipidemia [1]. In the last decades, an increase in dyslipidemia has been observed following rising the prevalence of overweight and obesity [2]. In 2008, the World Health Organization (WHO) reported that more than 1.4 billion adults were overweight. Of these, more than 500 million subjects were obese [3]. Weight management interventions are basically aimed at reducing dietary energy intake in combination with physical activity, life style modifications and recently pharmacotherapy [4]. Given difficulties in adherence to dietary recommendations for weight maintenance, obese and overweight subjects often turn to drugs and supplementations. More recently, there has been a greater focus on medicinal plants to ensure weight reduction [5].

Previous studies provided evidence on anti-obesity properties of many edible plants such as green tea, pepper, *Camellia synensis* [6] and *Glycyrrhiza glabra* [7]. The *G. glabra* root (Licorice) is one of frequently used medicinal herbs in the traditional medicine. *G. glabra* root has been suggested to possess many

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therapeutic and medicinal characteristics including antiviral activity, relief of peptic ulcer diseases and antioxidant/anti-inflammatory effects [8]. These effects are partly attributed to glycyrrhizin, glabrol, glabridin, flavenoid fractions and volatile components of the herb [8].

Some research has suggested that licorice root could be effective in reducing abdominal fat deposition and improving lipid profile. Fuhrman et al. [9] suggested that licorice root extract consumption reduced total cholesterol (TC) and low-density lipoprotein (LDL) in moderately hypercholesterolemic patients. Also, Tominaga et al. [10] reported that licorice flavenoid oil (LFO) reduced LDL-levels after 8 weeks in overweight subjects. Whilst, Bell et al. [11] trial did not find any effect of LFO on lipid profile in overweight/obese subjects and athlete men after 8 weeks.

In summary the above reports, the effects of licorice root on the lipid profile remains contradictory and it is difficult to make a conclusion about the effects of licorice on dyslipidemia. In addition, it seems that no study has been conducted to compare the concurrent effect of supplementation with Licorice and low-calorie diet to low-calorie diet alone on lipid profile and weight loss. Therefore, the aim of the present study was to elucidate the effects of dried extract licorice along with a low calorie diet on lipid profiles in overweight and obese subjects.

Materials and methods

Participants and study design

A randomized double-blind clinical trial was conducted on 64 overweight and obese volunteers (27 men, 37 women). The sample size was calculated based on the fat mass variables in Tominaga et al's study and with α-value 0.05, power 90% and considering 20% loss to follow up, subjects were recruited by dietitian referral from March to September 2013 at Sheikhoraees clinic affiliated to Tabriz University of Medical Sciences, Tabriz, Iran. Inclusion criteria were as follows: age 30–60 years old and body mass index (BMI) > 25 kg/m^2. Exclusion criteria were CVD, liver, thyroid and kidney disorders, diabetes mellitus, smoking, receiving any anti-obesity medications, vitamin–mineral supplements or herbal drugs, pregnancy and lactation.

At the beginning of the trial, general characteristics including age, medication history, obesity history and dietary habits were collected. The trial was approved by the Ethics Committee of Tabriz University of Medical Sciences and a written informed consent was obtained from each patient. The trial was registered on the Iranian Registry of Clinical Trials (www.irct.ir/, IRCT2013062811288N3).

Randomization and allocation

Eligible participants were randomly assigned into intervention ($n = 32$) or placebo groups ($n = 32$). Randomization facilitated by random number tables with a permuted block size of two. To ensure double blinding, the allocation was performed by an investigator with no clinical involvement in the study and principal investigators remained masked to the treatment assignments until data collections were completed. Besides, both researchers and the participants remained blind for randomization and allocation until final data analyses. Further, all the participants were stratified for sex, age and BMI.

Intervention

All the participants received a low calorie diet. A dietitian designed an individualized diet to reduce energy intake by 500 kcal from the total energy requirement. Resting energy expenditure was calculated using Mifflin equation [12]. Prescribed diet contained 55% carbohydrate, 15% protein and 30% fat. Intervention and placebo groups took 1.5 g/day (divided into three times a day 30 min before each meal) of dried licorice extract and placebo (corn starch), respectively, for 8 consecutive weeks. Follow up visits were arranged in 20-days intervals. Supplements were distributed among the volunteers based on the allocation code after the randomization. In order to minimize subjects' withdrawal and as an advocacy approach all the participants received serial weekly phone calls. Throughout the trial, the subjects were asked to maintain their usual physical activity levels. The patients also had the option to quit the study anytime during the intervention. Finally, adherence to the study protocol was assessed by number of returned capsules.

Preparation of licorice extract and placebo

The licorice extract was prepared by Darook pharmacological company (Esfahan, Iran) with registered number of 1228104305. Briefly, it was a dried hydroalcoholic extract of licorice root (ethanol 70:water 30% v/v) containing lowered glycyrrhizin (<0.01%). Glycyrrhizin was separated from the extract using ultrafiltration. The ultrafiltration device included a membrane which was able to selectively separate the glycyrrhizic acid from other components. The yield of the extraction was 10% (10 g extract/100 g powdered licorice root). Corn starch as placebo and licorice extract was filled in capsules in same size and color. Both licorice extract and placebo capsules were provided in the same opaque pockets. They were coded by the company and the researchers and the participants were masked for type of intervention until the data were analyzed.

Assessments

Assessments were included anthropometric indices, dietary intake, physical activity level and biochemical measurements at baseline and at the end of study.

Weight was measured with minimum clothing without shoes to the nearest 0.1 kg. Height was measured without shoes using the SECA stadiometer to the nearest 0.1 cm by a trained staff. Body mass index (BMI) was calculated by dividing the weight in kilogram to square with height in meter. Based on WHO classification, subjects with BMI of 25–29.9, 30–34.9 and 35–39.9 kg/m^2 were considered overweight, grade I obese and grade II obese, respectively. 24-h dietary record questionnaires (2 work days and 1 weekend) were filled out by patients at the