



Research paper

The effect of artichoke leaf extract supplementation on lipid and CETP response in metabolic syndrome with respect to Taq 1B CETP polymorphism: A randomized placebo-controlled clinical trial

Khatereh Rezazadeh^{a,c}, Farzin Rezazadeh^b, Mehranghiz Ebrahimi-Mameghani^{c,*}

^a Talented Students Center, Student Research Committee, School of Nutrition & Food Sciences, Tabriz University of Medical Sciences, Tabriz, Iran

^b School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

^c Nutrition Research Center, School of Nutrition & Food Sciences, Tabriz University of Medical Sciences, Tabriz, Iran

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ABSTRACT

Introduction: The potentially favorable effects of artichoke leaf extract (ALE) have been shown on lipid profile; however, results are inconsistent. Taq IB polymorphism in cholesteryl ester transfer protein (CETP) gene may modulate the response to intervention. This study was aimed to examine the effects of ALE supplementation on serum lipid profile and CETP levels regarding CETP Taq IB polymorphism in patients with metabolic syndrome (MetS).

Methods: In this double-blind placebo-controlled clinical trial, 80 patients with MetS were randomized to receive ALE (1800 mg per day as four tablets) or matching placebo for 12 weeks. Serum levels of lipid profile and CETP, as well as physical activity levels were assessed before and after the intervention. Physical activity levels were measured using short form of the International Physical Activity Questionnaire (IPAQ-SF). Moreover, patients were genotyped for CETP Taq IB polymorphism.

Results: Mean age and BMI of the patients was 38.91 ± 6.90 years and 34.32 ± 4.28 kg/m² respectively. Twenty-eight percent of the patients were male. ALE supplementation decreased serum triglyceride (TG) level compared to placebo over 12 weeks (-10% vs. -2% , $p = 0.01$). There was no interaction between CETP Taq IB genotype and response to ALE supplementation. The subgroup analysis showed that in men carriers of Taq IB-B1B1, LDL-C level significantly decreased in ALE group compared to the placebo group (-15% vs. 9% , $p = 0.004$).

Conclusions: ALE supplementation decreased TG levels without intervention-genotype interaction in patients with MetS. However, men with Taq IB-B1B1 genotype indicated a reduction of LDL-C in response to ALE.

1. Introduction

Artichoke (*Cynara Scolymus* L.) is a member of Asteraceae family and its leaves are extensively used both as a food and medicine [1]. Artichoke Leaf Extract (ALE) has been traditionally used in the treatment of hepato-biliary diseases and dyspepsia. Previous studies have revealed various pharmacological activity of ALE including hepatoprotective [2], antimicrobial [3], antiatherogenic [4], antioxidant [2,5], hypoglycemic [6,7] and anticancer [8] effects. The hypolipidemic properties of ALE and its compounds has also been recently noticed [7,9–11], which are mediated through choleretic effects [12] and the inhibition of cholesterol biosynthesis [13]. The main phytochemical compounds of ALE appears to be caffeoylquinic acids (e.g.

chlorogenic acid, cynarin), caffeic acid, sesquiterpene lactones and flavonoids (luteolin, luteolin 7-o-glucoside) [1,14]. There is evidence indicating that ALE is well-tolerated without any serious side effects [7,10,15] and mutagenic or genotoxic effects [16].

Metabolic syndrome (MetS) is defined as the clustering of abdominal obesity, hypertension, hyperglycemia, and dyslipidemia (lowered high-density lipoprotein cholesterol (HDL-C) and raised triglycerides (TG) levels) [17], which can increase the risk of developing cardiovascular diseases (CVD) [18]. The rising prevalence of MetS is recognized as a major public health concern over the world [17]. Therefore, improving lipid profile could decrease CVD risk in the afflicted patients.

The cholesteryl ester transfer protein (CETP) is a hydrophobic

Abbreviations: ALE, artichoke leaf extract; CETP, cholesteryl ester transfer protein; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference

* Corresponding author at: Nutrition Research Center, School of Nutrition & Food Sciences, Tabriz University of Medical Sciences, Attar Neyshaboori Av Golghasht St Tabriz, Iran.

E-mail address: ebrahimimamagani@tbzmed.ac.ir (M. Ebrahimi-Mameghani).

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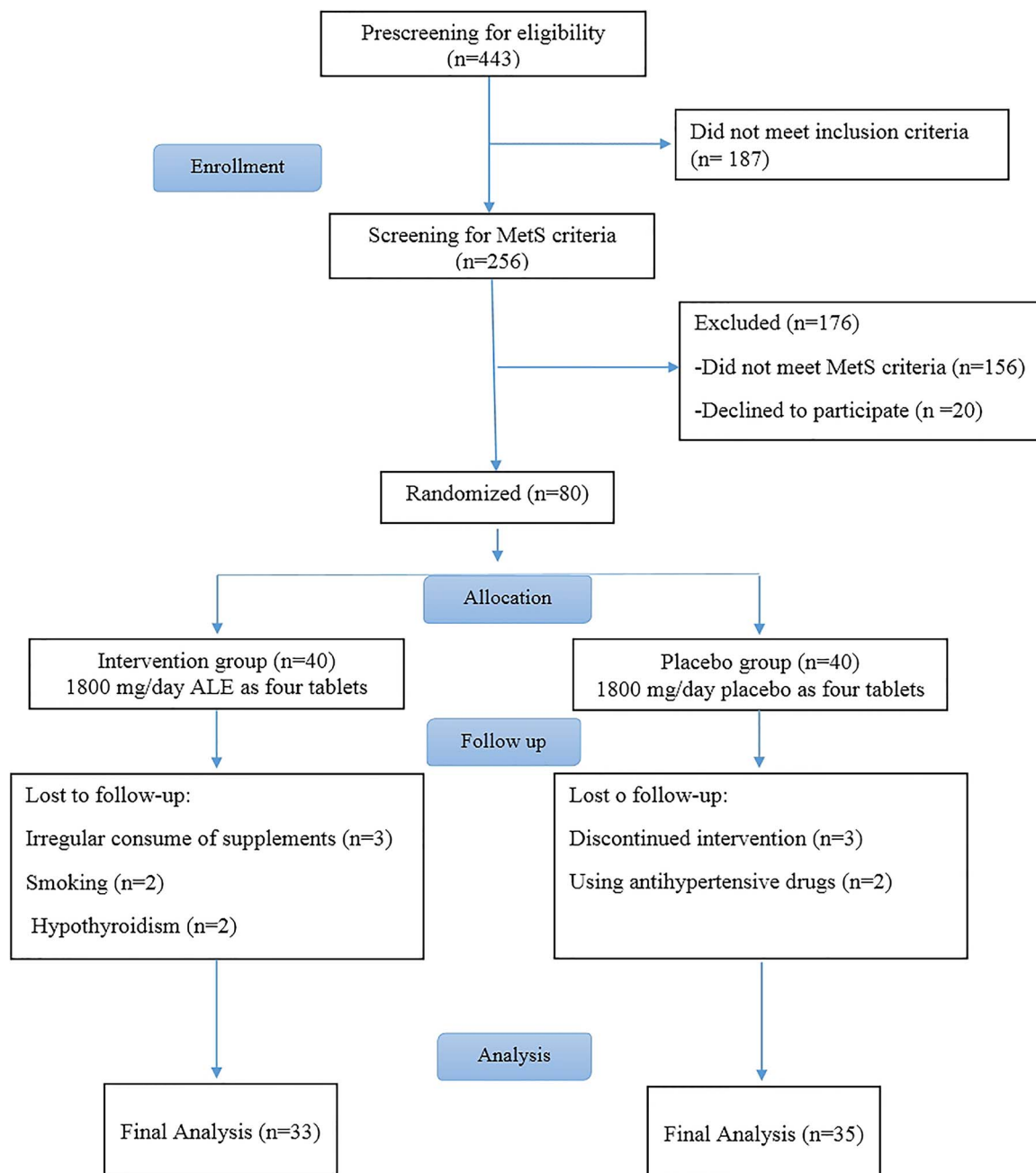


Fig. 1. Flow diagram of the study.

glycoprotein with a key role in lipid metabolism via mediating the exchange of cholesteryl ester (CE) and TG between cholesterol-rich lipoproteins and TG-rich lipoproteins [19]. In a study, a significant association between the increase of CETP mass and MetS was found in men [20]. Most of the published literature suggests that Taq-IB (rs708272), a common polymorphism in intron 1 of the CETP gene, is related to the risk of CVD and response to lipid lowering therapy, however the latter has not been confirmed yet [21]. The carriers of the B2 allele have shown an increase in HDL-C levels and a decrease in TG levels, CETP activity, and MetS risk [22,23].

The promising effects of ALE on lipid metabolism [7,9–11], and the possibility of the modulation of the response to ALE by individuals' genetic differences [24] have been already recognized. However, to best of our knowledge, the efficacy of ALE on CETP concentration and the variability in response, considering Taq IB polymorphism is yet to be studied. Therefore, the present study was aimed to examine the

effects of ALE on lipid profile and CETP concentration in patients with MetS, considering the modulation of the response by Taq IB polymorphism.

2. Materials and methods

2.1. Subjects

This study was conducted on patients with MetS ($n = 80$) in Khoy, Iran. The diagnosis of MetS was based on the international criteria, i.e. having at least three out of the five criteria, as follows: TG ≥ 150 mg/dl, fasting blood sugar (FBS) ≥ 100 mg/dl, HDL-C < 40 mg/dl for men and < 50 mg/dl for women, systolic blood pressure (SBP) ≥ 130 and/or diastolic blood pressure (DBP) ≥ 85 mg/dl, and waist circumference (WC) ≥ 95 cm in both sexes [25]. The cut-off point for WC was determined based on a report of the Iranian National Committee of

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