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Lipid-modifying effects of adjunctive therapy with curcuminoids—piperine combination in patients with metabolic syndrome: Results of a randomized controlled trial

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Turmeric

Summary
Background: Dyslipidemia is an established feature of metabolic syndrome (MS) that is associated with an increased risk of atherosclerotic cardiovascular disease. Curcuminoids are natural products with anti-atherosclerotic and lipid-modifying effects but their efficacy in patients with MS has not yet been tested.
Objective: To investigate the effects of bioavailability-enhanced curcuminoids, as adjunctive to standard of care, on serum lipid concentrations in patients with MS.
Methods: Patients diagnosed with MS according to the NCEP-ATPIII criteria who were receiving standard of care were assigned to either curcuminoids (C3 complex®; 1000 mg/day; $n = 50$) or placebo ($n = 50$; matched with drug capsules in shape and color) for 8 weeks. In order to improve the oral bioavailability, curcuminoids were co-administered with piperine (bioperine®) in a ratio of 100:1. Serum concentrations of total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, small dense LDL (sdLDL), lipoprotein(a) [Lp(a)], and non-HDL-C were determined at baseline and at the end of 8-week treatment period.

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Results: Curcuminoids were more effective than placebo in reducing serum LDL-C, non-HDL-C, total cholesterol, triglycerides and Lp(a), and elevating HDL-C concentrations. However, changes in serum sdLDL levels were found to be comparable between the study groups. The effects of curcuminoids on triglycerides, non-HDL-C, total cholesterol and Lp(a) remained significant after adjustment for baseline values of lipids and body mass index.
Conclusion: Curcuminoids—piperine combination is an efficacious adjunctive therapy in patients with MS and can modify serum lipid concentrations beyond what is achieved with standard of care.

Introduction

The metabolic syndrome (MS) is a cluster of several interrelated cardiometabolic risk factors including abdominal obesity, hyperglycemia/impaired glucose tolerance, hypertension and atherogenic dyslipidemia.[1] Constellation of these risk factors puts the affected patient at an increased risk of type 2 diabetes and atherosclerotic cardiovascular disease (ACVD).[2] MS has been the focus of increasing attention over the past few years owing to its rapidly increasing prevalence that is nearing epidemic proportions in Western societies.[3] The cornerstone in the management of MS is controlling the individual risk factors. Dyslipidemia is a key yet modifiable risk factor of MS. The predominant type of dyslipidemia in patients with MS is atherogenic dyslipidemia, which is characterized by elevated plasma triglyceride and low high-density lipoprotein cholesterol (HDL-C) levels.[4] Moreover, MS is most often associated with a preponderance of small dense low-density lipoprotein (sdLDL) particles, a subfraction of LDL that is more susceptible to oxidation, and triggering foam cell formation and atherogenesis.[5] Based on the recent guidelines, the primary goal in the management of dyslipidemia in MS is to achieve an optimal, yet strict, plasma LDL-cholesterol (LDL-C) levels of <70 mg/dL.[6] This is due to the strong and unequivocal association of LDL-C with ACVD outcomes in large trials, and the established efficacy of LDL-C reduction in both primary and secondary prevention of ACVD. Secondary lipid goals in MS patients include reducing plasma non-HDL-C and triglycerides, and elevation of HDL-C.[7]

The efficacy of statins, as the first-choice and the most potent class of LDL-lowering agents, in achieving LDL-C targets and modulation of features associated with atherogenic dyslipidemia is limited. Therefore, a considerable proportion of statin-treated MS patients require combination therapy with fibrates or niacin. However, such combinations would introduce additional problems owing to the potential interactions, and more importantly, adverse events such as flushing (with niacin) and risk of myopathies, and hepatic and renal dysfunction (with statin—fibrate combination therapy).[8] These limitations necessitate further research to find effective lipid-modifying treatments that could be used as adjunctive to statin therapy in MS and associated comorbidities.[9—16]

Curcuminoids are polyphenolic phytochemicals and active ingredients of the famous dietary spice turmeric. Curcuminoids have been extensively studied in relation to their therapeutic efficacy in different disease models.[17,18] To date, numerous pharmacological activities have been identified for curcuminoids in preclinical and clinical models, nominating these phytochemicals as a multifunctional supplement for several diseases.[17—30] The versatility of medicinal properties of curcuminoids is due to their potential to interact with a wide spectrum of molecular targets such as enzymes, receptors, transcription factors, growth factors, hormones, cytokines, adipokines and adhesion molecules.[31] Notably, curcuminoids have been shown to modulate several features of MS by improving insulin sensitivity,[32,33] suppressing adipogenesis,[34] reducing elevated blood pressure[35] and mitigating inflammation[22,36] and oxidative stress.[37,38] Moreover, there is evidence indicating that curcuminoids modulate the expression of genes and activity of enzymes involved in lipoprotein metabolism, and through which reduce plasma triglycerides and cholesterol,[39—41] and elevate HDL-C concentrations.[42] In spite of such a strong mechanistic rationale,[43] the efficacy of curcuminoids has not yet been tested in a clinical trial in MS patients. The objective of the present study was to investigate the clinical efficacy of a unique curcuminoid formulation as adjunctive to standard of care in patients with MS.

Materials and methods

Subjects

Participants were selected from those referring to the Cardiology or Endocrinology Clinics of the Baqiyatallah Hospital (Tehran, Iran) from May 2013 to January 2013. Inclusion criteria were subjects from both genders aged 25—75 years, who fulfilled diagnostic criteria for MS based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) guidelines a follows: ≥3 of the following conditions: waist circumference ≥102 cm (male) or ≥88 cm (female), blood pressure ≥130/85 mmHg, triglycerides ≥1.7 mmol/L, HDL-C <1.03 mmol/L (males) or <1.29 mmol/L (females), fasting plasma glucose (FPG) ≥6.1 mmol/L.[44]

Exclusion criteria were pregnancy and breastfeeding, non-compliance with the study medication (defined as not using the medication for >1 week), participation in a concomitant trial, hypersensitivity to the study medication, presence of malignancies and Impossibility to give informed consent. The study protocol was reviewed and