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The Effect of Curcumin on HDL Cholesterol Uptake Capacity in Obese Individuals: A Pilot Study

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ABSTRACT

Introduction: Obesity is a common risk factor associated with cardiovascular disease (CVD) risk. Curcumin has been reported to exert beneficial effects on lipid metabolism, including HDL functionality. We have examined the effects of curcumin on HDL cholesterol uptake capacity in subjects with obesity.
Materials and Methods: 30 obese individuals received curcumin and placebo 1 g per day for a period of 30 days. The subjects were crossed over to the alternative regimen after a 2-week washout period. A modified cholesterol uptake capacity (CUC) assay was used to determine serum HDL functionality.
Results: The study groups had similar base line characteristics. We did not find significant effects (p>0.05) of curcumin on serum HDL CUC levels.
Conclusion: Curcumin administration at a dose of 1 g per day for 30 days did not affect HDL CUC in subjects with obesity.

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Introduction

The prevalence of obesity has increased in adults and children in several populations globally over the past three decades (1). The risk of several conditions is associated with obesity, including: metabolic syndrome (MetS), type 2 diabetes mellitus, insulin resistance, increased blood pressure, CHD,

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gallbladder disease, cancer, osteoarthritis, asthma, sleep apnea, psychological distress, menstrual irregularities and complications of pregnancy (Both genetic and environmental factors contribute to the etiology of obesity(2).

Whilst it has been shown that serum HDL is inversely associated with the risk of CVD, trials of drugs that increase HDL-C levels have not been shown to reduce CVD events (3). The heterogeneity in the particle composition of HDL that caused to need for finding confirmed assays of HDL function (4). Cholesterol efflux capacity (CEC) is a measure of HDL function. It has been shown that CEC from macrophages shows a robust inverse relationship with both carotid intima-media thickness and the probability of angiographic coronary artery disease (CAD), independently of the HDL-C concentration (5)

Curcumin, a polyphenol extracted from the turmeric plant (Curcuma Longa L.), [diferuloylmethane: C21H20O6], has been extensively studied for its biological activities and has many health benefits (6, 7) . Curcumin may affect HDL functionality because it is able to regulate both the level and the activity of markers of HDL function that include apolipoprotein A1, cholesteryl ester transfer protein, and lecithin: cholesterol acyl transferase, paraoxonase-1 and myeloperoxidase (8).

Despite the significant pharmacological potential of curcumin, the clinical effect of curcumin is limited by its low bioavailability, which is due to its unfavorable pharmacokinetic properties, i.e. low absorption, rapid metabolism, and excretion from the body and consequently its low plasma concentration (9). Researchers are currently looking for new formulations of the compound to improve its kinetics, which have higher absorption, lower removal and longer biological half-life than conventional curcumin

Since obesity associated to abnormal function of HDL and curcumin may modulate HDL functionality, in current research for the first time we aim to assess effect of curcumin on HDL functionality in subjects with obesity.

Methods

Design

This was a randomized clinical trial approved by the Mashhad University of Medical Sciences (ID: 960443). In preliminary study (IRCT2013082914521N1) (10), 30 subjects with obesity aged 18-65 years who referred to Nutrition Department of Ghaem Hospital, Mashhad, Iran, were enrolled from August 2010 to August 2012. Informed consent forms were signed afterward the protocol explanation to all subjects. Inclusion/exclusion criteria have been defined before (10). Obesity was defined as BMI >30 kg per m^2 and subjects were not taking a lipid-lowering agent and other drugs that may alter lipid metabolism.

The random allocation to group was made using computer randomization. Sequentially numbered sealed envelopes were used to implement the random allocation sequence which opened by a person not involved in the project. The participants, clinical research staff and statistician were blinded after assignment to intervention. So that, the capsules containers were coded as A and B by a non-researcher person and remained confidential until data analysis. Moreover, the placebo capsules were similar to the curcumin ones concerning the shape, weight and color. All individuals took curcumin or placebo (n=15; in each study group) 1 g per day for a period of 30 days. There was then a 2-week wash-out period, after which subjects were crossed over to the alternate regimen.

Curcumin capsules contained 500 mg as curcuminoids plus 5 mg bioperine, were acquired (Sami Labs LTD, Bangalore, India) (11). Placebo capsules that contained 5 mg piperine were of the same in shape and color as the curcumin capsules.

All subjects completed a questionnaire including demographic information. As well, anthropometric indices were measured using standard protocols.

Serum biochemical variables

A 12 hours fasted blood sample was taken 4 times from every subject at baseline and after each period. Serum lipid profile and fasting blood glucose (FBG) determined using Pars Azmoon kits (Tehran, Iran).

HDL functionality

A modified cholesterol uptake capacity (CUC) assay (12), was used to determine serum HDL functionality. The inter-assay and intra- assay CV were 13.07% and 6.65%, respectively.

ApoB depleted serum was incubated with fluorescent-labelled (BODIPY) cholesterol. Then, a monoclonal antibody against apolipoprotein A1 (ApoA1) that coated on microplate used to capture HDL. The BODIPY-cholesterol uptake through HDL was measured followed after numerous washing.

Two parameters for CUC value were defined as follows: CUC %: BODIPY-cholesterol uptake percent by apoB depleted sample; as well N-CUC: normalized CUC with HDL-C level (13).

Statistical analysis

Raw data were prepared for analyzing with the Statistical Analysis Software (SPSS version 16) formerly; the t-test and Mann-Whitney U test were used for normally and non-normally dispersed factors, respectively. The carry over effects, treatment and period were evaluated for 2_2 crossover study. A two-sided P-value <0.05 were considered to be statistically significant.

Results

It is a randomized double-blind crossover trial. The base line clinical features of the study population summarized in Table 1. No significant differences were found for baseline characteristics of two groups (p> 0.05). There was no statistical significant effect (p>0.05) of curcumin supplementation (1g per day for 30 days) on serum HDL functionality in two groups (Table 2).

Table 1: Clinical characteristics of the subjects

Variables	Curcumin& Placebo	Placebo& Curcumin	P-value
Age, years	38.84±11.12	37.81±12.31	0.09
Body Mass Index	33.95±3.80	32.65±4.69	0.37
Systolic Blood Pressure (mmHg)	118.84±13.29	117.62±10.99	0.77
Diastolic Blood Pressure (mmHg)	79.63±10.21	80.44±8.41	0.80
Serum Lipid concentrations			
HDL-C (mg/dl)	46.8±9.55	46.12±7.77	0.80
LDL-C (mg/dl)	119.79±23.15	118.75±27.72	0.90
Cholesterol (mg/dl)	193.10±29.16	188.94±27.63	0.67
Triglyceride (mg/dl)	105.05±30.22	124.94±55.44	0.19
Hs-CRP (mg/dl)	8.44±3.19	8.35±2.62	0.93

* Mean ± standard deviation for continuous variables

Table 2: Curcumin's effect on cholesterol uptake capacity in population study

		N	1st period		2nd period		P-value			
Variable	**Study group**		Pre treatment	Post treatment	Pre treatment	Post treatment	Period effect	Treatment effect	First effect of carry over	Second effect of carry over
Cholesterol uptake capacity % (a.u.)	**Curcumin&Placebo**	15	0.88(0.19)	0.83(0.26)	0.89(0.46)	0.79(0.24)	0.46	0.79	0.24	0.77
	Placebo&Curcumin	15	0.92(0.51)	0.90(0.34)	0.76(0.14)	0.74(0.26)				

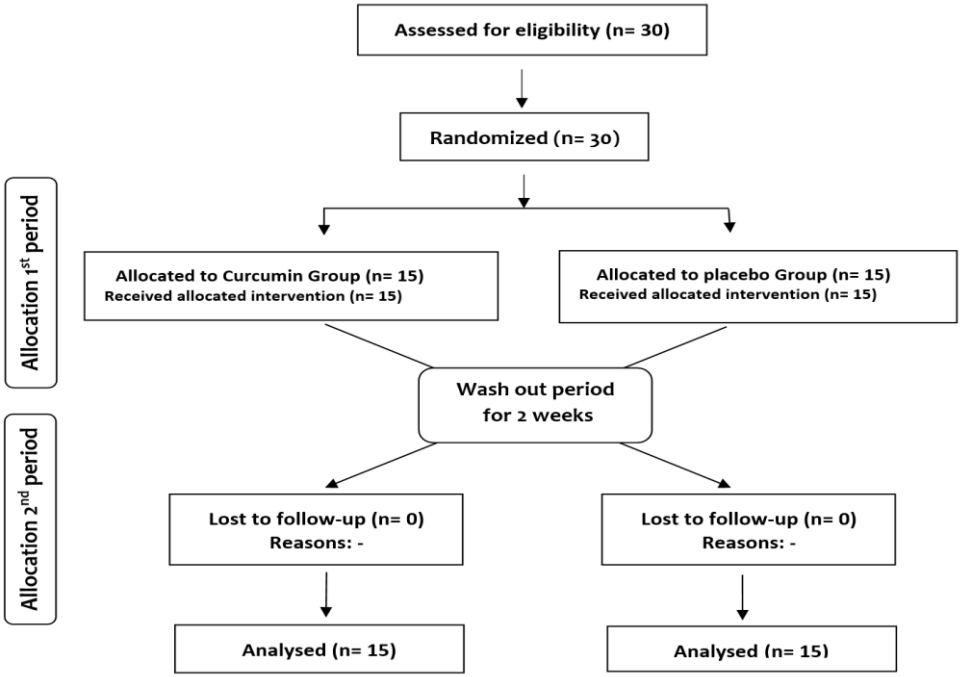

Figure 1: Flow chart of trial

Discussion

This study is the first evaluation of curcumin effect on HDL cholesterol uptake capacity in obese subjects. The results indicated that curcumin supplementation by 1 g per day for 30 days have no significant effect on HDL functionality in subjects with obesity.

We previously showed that curcumin supplementation (1 g/day) for a period of 6 weeks was tolerated and safe in patients with metabolic syndrome (14, 15). The study of Yang et al. has indicated increased HDL-C level significantly using curcumin at a dose of 630 mg per day for 12 weeks among 33 subjects with metabolic syndrome (16).

While Baum et al. have found supplementation of curcumin with 4 g per day curcumin, 1 g per day curcumin, for 6-month in 36 individuals did not have any significant effect on HDL-C (17)

Janga et al. have indicated plasma HDL-C can be significantly increased by curcumin in hamsters with high fat diet for 12 weeks (18). Also, an investigation meta- analyses by Sahebkar et al. did not find curcumin beneficial effects on lipid profile such as HDL-C (19) but other meta-analyses studies have confirmed elevated level of HDL-C by curcumin supplementation (20). Different results in previous studies of the effects of curcumin on serum lipid levels may be related to short duration of studies, low dosages of curcumin, different diseases of populations under investigation (background diseases), also using unformulated supplements of curcumin which have lower intestinal absorptive capacity and bioavalability. The other reason for these differences might be correlated to stage of the disease. Studies have been shown lipid profile in subjects might not remarkably change to normal range in the first stage of disease (20). Previous studies have been indicated lipid lowering effects of curcumin by decreasing cholesterol uptake in the intestinal track and modulating enzymes, which contribute to lipid profiles homeostasis. The cholesterol efflux by inducing ABCA1carreir expression may be stimulated with curcumin (20).

Javandoost et al., examined the effects of curcumin and curcumin phosphatidylcholine complex on CETP in patients with metabolic syndrome. Subjects divided into three groups and each group comprised 40 individuals. One group received curcumin, one group received phytosomal curcumin and the other group received placebo for 6 weeks. They found that curcumin phosphatidylcholine complex has higher bioavailability by pretending to cell membranes (21). Previous studies found most of curcumin effects in lowering lipid profiles can be exerted with doses > 1 g and duration >8 weeks (20).

However, in this study, we used curcumin-piperine complex and it received for 30 days so did not show significant effect on HDL functionality.

The strength points of our study were its crossover design and the first human investigation of curcumin effect on HDL functionality. Weakness points were using one dosage, one curcumin formulation, and short period of the study.

Conclusion

We have found that a short period of curcumin supplementation has no significant impact on HDL cholesterol uptake capacity. Future investigations have to consider different dosages of curcumin, better formulation, larger population and longer duration of study.

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Ethical statements

Informed consent was obtained from all individual participants included in the study.

Conflict of Interest statement

The authors confirm no conflict of interest.

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