Austin Journal of Obesity & Metabolic Syndrome

Open Access

Austin Publishing Group

Research Article

Effect of Curcumin Supplements on Serum Cell Adhesion Molecule (CAM) Concentrations in Obese Subjects

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Received: May 15, 2020; **Accepted:** June 09, 2020; **Published:** June 16, 2020

Abstract

Background: Obesity is associated with an increased risk of several diseases including Cardiovascular Disease (CVD) and metabolic syndrome (MetS). It has been shown that increased serum concentrations of some Cellular Adhesion Molecules (CAMs) indicate systemic inflammation, and is associated with an increased risk of atherosclerosis. The aim of this study was to assess the effect of curcumin supplements on serum CAMs in obese individuals.

Methods: A randomized double-blind crossover design was used. Obese participants (aged 36.18±12.88 years old) were enrolled from our previous work. All subjects received curcuminoids or placebo 1 g/day for a period of 30 days. After 2-weeks wash-out, participants were crossed over to the other regimen. Anthropometric measurements were determined using standard protocols. ELISA kits were used to measure serum soluble ICAM-1, VCAM-1, L- and P-selectin. SPSS software was used for the statistical analysis.

Results: The results showed that serum VCAM-1 concentrations were reduced by 1 g/day curcumin supplementation for a period of 30 days (p=0.05). However, there was no significant effect of the curcumin supplement on serum L-selectin, P-selectin or ICAM-1 (p>0.05 for all variables), and no carry-over effect between the trial periods in the studied groups (p>0.05 for all factors).

Conclusions: The results can suggest that curcumin supplementation at dose of 1 g/day can reduce serum VCAM-1 concentrations in obese subjects.

Keywords: Curcumin; Obesity; Adhesion Molecules

Introduction

Obesity is a global problem and is associated with an increased risk of several diseases including CVD, MetS, cancers, diabetes mellitus and hypertension Obesity is associated with a chronic, low grade inflammation that has been called metabolic inflammation [1-4]. Adipose tissue secrets bioactive proteins called adipokines that are pro-inflammatory [5] and may in part account for the increased risk of atherosclerosis [4].

Cellular Adhesion Molecules (CAMs) are proteins located on the cell surface and are up-regulated by inflammation. An increased expression of CAMs is associated with an increased risk of atherosclerosis and cancers. Soluble Intercellular Adhesion Molecule (ICAM), Vascular Cell Adhesion Molecule (VCAM), Endothelial Selectin (E-Selectin), Leukocyte Selectin (L-Selectin), Platelet Selectin (P-Selectin) are found in serum [6-9]. E and P-Selectin play a role in the pathogenesis of atherosclerosis as mediators of leukocytes migration to vascular endothelial cells. ICAM and VCAM play a role in the pathogenesis of atherosclerosis as mediators of leukocyte recruitment and platelet adhesion [10-12] Obesity is associated with an increase in serum CAMs, and a, reduction of CAMs may therefore indicate a lowering of risk of the diseases in the obese subjects [13,14].

Curcumin is a polyphenol and effective ingredient of Curcuma Longa (turmeric). Curcumin has been reported to have many health and therapeutic properties and previous evidence has shown that it has strong anti-inflammatory and anti-oxidant properties [15]. Previous animal studies have shown the anti-atherosclerotic effect of curcumin and its effect on the expression of CAMs [16]. The purpose of this current study was to evaluate the effect of curcumin on CAMs that have been related to the pathogenesis of atherosclerosis, in obese subjects. To enhance the bioavailability of curcumin, piperin was co-administered. Piperin is an active ingredient present in black pepper, and a natural compound that increases the bioavailability of curcumin [17].

Methods

Study design

Twenty-one obese participants were recruited into this randomized double-blind crossover trial. They were aged 18-65 years old having a BMI≥30 (kg/m^2) [18]. All subjects received curcuminoids (n=5) or placebo (n=8) 1 g/day for a period of 30 days. After 2-weeks wash-out, they finally crossed over to the different regimen. Inclusion and exclusion criteria have been described in detail previously [18]. Curcuminoid capsules were purchased from Sami Labs LTD (Bangalore, India), and comprised 500mg as C3 Complex® curcuminoids +5mg bioperine®. Placebo capsules were identical in appearance, and contained 5 mg piperine alone.

Demographic and Anthropometric data

All volunteers were asked to complete a questionnaire to provide information on their socio-demographic status, smoking behavior

Citation: Saberi-Karimian M, Rezaei M, Ghazizadeh H, Nikbakht-Jam I, Orooji A, Tavallaie S, et al. Effect of Curcumin Supplements on Serum Cell Adhesion Molecule (CAM) Concentrations in Obese Subjects. Austin J Obes & Metab Synd. 2020; 4(1): 1014.

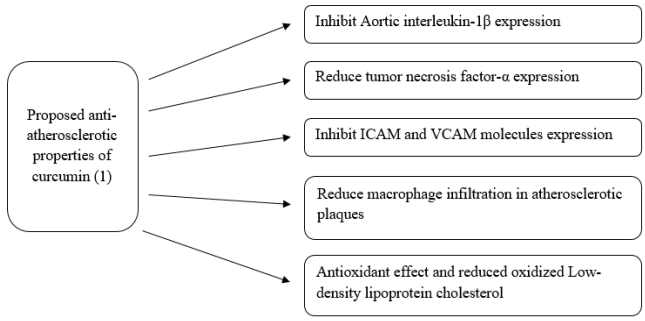

Figure 1: Anti-atherosclerotic properties of curcumin.

and medical history. Anthropometric indices including weight, height, waist circumference, and fat percentage were determined using standard protocols. BMI was defined as weight (kg) to height (m^2) ratio.

Serum biochemical factors

Fasted blood samples (12h) were taken 4 times from all participants before and after every period. Serum fasting blood glucose, lipid profile [triglycerides, total cholesterol, High-Density Lipoprotein Cholesterol (HDL-C) and low-density Lipoprotein Cholesterol (LDL-C)] were determined enzymatically using commercial kits (Pars Azmoon, Tehran, Iran) in all samples.

Human ELISA kits were used to measure ICAM-1, VCAM-1(ORIGENE, Rockville, USA), L- and P-selectin (Sigma Aldrich, Saint Louis, USA) in all samples.

Statistical analysis

The data analysis was done with the Statistical Analysis Software (SPSS version 20). The Student's t test used for normally distributed variables. For 2_2 cross-over study was used to assess the effect of carry over, treatment and period. A two-sided p value of <0.05 was considered statistically significant. Data were assessed for normality using the Kolmogorov-Smirnov test, and were expressed as means±SD (for normally distributed data) or median and interquartile range (for non-normally distributed data).

Results

General features of participants in the study

Anthropometric indices and serum levels of lipids profile of the participants (aged 36.18±12.88 years old) are described in Table 1. The mean values of age, height, weight, LDL-C, HDL-C, triglyceride, PAB, hs-CRP and BMI are mentioned in participants in details (Table 1).

Baseline and post-trial values for L-selectin, P-selectin, ICAM-1 and VCAM-1 in each study period are presented in Tables 2, respectively. The results showed that serum concentration of VCAM-1 is reduced by 1 g/day curcumin supplementation over a period of 30 days (p=0.05, power 53%). There was no significant effect of curcumin supplement on serum L-selectin, P-selectin and ICAM-1 concentrations (p>0.05 for all biochemical factors) as well as carry-over effect between the trial periods in studied groups (p>0.05 for all variable).

Discussion

This study conducted to evaluate the effect of curcuminoids (1 g/day for 30 days) on cell adhesion molecules of ICAM-1, VCAM-1, L-Selectin and P-Selectin among obese subjects in a randomized double-blind, placebo-controlled crossover trial. The results showed that curcumin supplementation (1 g/day) can improve the serum VCAM-1 during 30 days (p=0.05). But there were no significant effect

Table 1: Demographic variables and baseline clinical features.

Variables				
Group	Total populatioon	Curcumin & Placebo	Placebo & Curcumin	p-value
Age, years	38.37±11.51	38.84±11.12	37.81±12.31	0.09
Demispan (cm)	80.67±5.88	79.48±4.91	82.63±5.58	0.79
Height (cm)	160.54±8.17	158.5±6.36	159.94±9.63	0.6
Weight (Kg)	81.48±12.09	85.57±12.95	83.83±17.43	0.74
Waist circumference (cm)	106.31±10.72	110.34±10.41	106.53±10.42	0.29
Hip circumference (cm)	113.32±7.10	117.97±9.84	115.07±9.31	0.38
Arm circumference (cm)	33.71±2.82	34.46±2.64	33.47±3.15	0.32
Fat %	38.06±6.27	41.25±5.49	36.48±5.82	0.02
Body Mass Index	31.61±3.78	33.95±3.80	32.65±4.69	0.37
Systolic Blood Pressure (mmHg)	116.69±10.15	118.84±13.29	117.62±10.99	0.77
Diastolic Blood Pressure (mmHg)	78.15±7.76	79.63±10.21	80.44±8.41	0.8
HDL-C (mg/dl)	47.54±9.63	46.8±9.55	46.12±7.77	0.8
LDL-C (mg/dl)	118.23±30.18	119.79±23.15	118.75±27.72	0.9
Cholesterol (mg/dl)	194.77±35.84	193.10±29.16	188.94±27.63	0.67
Triglyceride (mg/dl)	124.92±53.17	105.05±30.22	124.94±55.44	0.19
Hs-CRP (mg/dl)	9.14±2.72	8.44±3.19	8.35±2.62	0.93

*Mean ± standard deviation for continuous variables; Frequency (%) for categorical variables. HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol. AB: First Curcumin Second Placebo. BA; First Placebo Second Curcumin.

Table 2: Effect of curcumin supplementation on serum level of L-selectin, P-selectin, ICAM-1 and VCAM-1 in population study.

Variable	Stydy group	First priod		Second priod		P.value			
		Pre- treatment	Post- treatment	Pre-treatment	Post- treatment	Period effect	Treatment effect	First effect of carry over	Second effect of carry over
L-selectin (ng/ml)	Curcumin & Placebo	9.08±10.82	13.65±5.06	10.16±6.8	2.12±6.54	P=0.006	P=0.09	P=0.46	P=0.63
	Placebo & Curcumin	7.24±4.95	12.85±10.14	14.23±10.83	9.4±12.39				
P-selectin (ng/ml)	Curcumin & Placebo	0.94±0.69	0.93±0.68	1.05±0.98	0.51±0.64	P=0.89	P=0.84	P=0.77	P=0.65
	Placebo & Curcumin	1.21±0.91	1.17±1.56	1.05±0.89	0.57±0.38				
ICAM-1 (ng/ml)	Curcumin & Placebo	48.14±18.49	61.40±18.38	57.67±55.23	11.06±33.82	P<0.001	P=0.73	P=0.88	P=0.18
	Placebo & Curcumin	84.90±68.27	48.64±4.85	79.32±4.97	77.93±6.15				
VCAM-1 (ng/ml)	Curcumin & Placebo	10.38±4.88	6.69±2.67	4.22±1.02	3.42±1.40	P<0.001	P=0.054	P=0.11	P=0.16
	Placebo & Curcumin	4.34±3.32	4.17±2.35	2.88±1.69	3.33±2.82				

AB: First Curcumin Second Placebo. BA; First Placebo Second Curcumin.

of the intervention on the reduction of the cellular adhesion molecules of ICAM-1, E-Selectin and P-Selectin in the obese participants.

Obesity is associated with some underlying causes of atherosclerosis including oxidative stress, inflammation and endothelial dysfunction [19,20]. Obesity increases insulin resistance and oxidized LDL, and subsequently predisposes obese people to inflammation and atherosclerosis [21]. In the process of developing atherosclerosis; cell adhesion molecules produced by endothelial and reduction of them can be indicator of a reduction in the risk of atherosclerosis in the obese people [20].

Some previous human and animal studies have shown anti-oxidant, anti-inflammatory and anti-atherosclerotic properties of curcumin [22]. Figure 1 shows the major proposed mechanisms for anti-atherosclerotic properties of curcumin. In this regard, in the current study the CAMs used as an indicator of anti-atherosclerotic effect of curcumin.

Gangali et al., in a crossover clinical trial investigated effect of curcumin (1 g/day for 4 weeks) on inflammatory factors of interleukin 1B, IL-4 and vascular endothelial growth factor in obese subjects. The results of their study indicated a significant decrease in the inflammatory factors [23]. Franco-Robles et al., found that curcuimin at dose of 500 mg/day for 12 week associated with significant decrease in the lipid and protein oxidation [24]. The mentioned studies have shown the anti-inflammatory and anti-atherosclerotic effects of curcumin in similar dose of current study [22-24], but significant decrease in CAMs, which is expected to be associated with a reduction in inflammation, was not observed in our study. However, the change in CAMs is not the first approach of predisposing obese subjects to atherosclerosis, and earlier there is an increase in the LDL-oxidized and inflammatory factors which the previous studies have shown the effect of curcumin on reduction of them.

As far as we know before this study, no human studies conducted on the effect of curcmin on the cell adhesion molecules in the obese subjects. The main limitations of this study are the low sample size and short duration of the intervention, and the main advantage of this study is its cross-over method. Increasing the duration of the intervention, changing the dosage or formulation of the drug and increasing the sample size suggested for subsequent studies.

Conclusion

In this crossover clinical trial, curcumin at dose of 1 g/day for 4 weeks improved the serum VCAM-1 levels in the obese subjects whereas, did not result in significant reduction of other cell adhesion molecules. Changes in duration of intervention, and drug formulation and increase sample size suggested for further studies.

Acknowledgement

Dr. Maryam Saberi-Karimian is a post-doctoral fellow of Mashhad University of Medical Sciences (MUMS), which her fellowship being granted by MUMS, Iran.

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