Trends in Medical Research

ISSN 1819-3587

Academic Journals Inc.

www.academicjournals.com

OPEN ACCESS Trends in Medical Research

ISSN 1819-3587
DOI: 10.3923/tmr.2016.82.87

Research Article

Curcumin Intake Could Lower Serum Macrophage Migration Inhibitory Factor and Monocyte Chemoattractant Protein-1 Levels in Obese Subjects

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Abstract

Controlling of inflammatory process associated with obesity is a big challenge. Both Monocyte Chemoattractant Protein-1 (MCP-1) and macrophage Migration Inhibitory Factor (MIF) may play a role in this process. Aim to evaluate serum MPC-1 and MIF levels in obese subjects and detect the effect of oral curcumin intake. The study included 60 obese subjects (30 children and 30 adults). The trial subjects received a 500 mg curcumin capsule with the main meal for 4 weeks. Controls received a placebo capsule for 4 weeks. A total of 60 normal weights enrolled as controls. The MIF and MCP-1 levels were measured on days 1 and 29 using commercially available ELISA kits. The mean serum level of MPC-1 and MIF were significantly higher in obese group than in controls. Curcumin intake resulted in statistically significant decrease in serum MPC-1 and serum MIF in children and adults. Our results showed that curcumin could help in lowering MIF and MPC-1 associated with obesity. It could help in prevention of obesity complications.

Key words: Obesity, MIF, MPC-1, curcumin

Received: December 19, 2015 Accepted: February 03, 2016 Published: March 15, 2016

Citation: Nagwa Abdallah Ismail, Soha M. Abd El Dayem, Mona Hamed, Dina F. Ayoub, Eman Mahmoud Hassan and Heba Assal, 2016. Curcumin intake could lower serum macrophage migration inhibitory factor and monocyte chemoattractant protein-1 levels in obese subjects. Trends Med. Res., 11: 82-87.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

The prevalence of obesity is increasing rapidly in most countries and is an urgent public health problem (Black *et al*., 2013; Ng *et al*., 2014). Complications of obesity are a big problem nowadays. Obesity is associated with many health complications and an increased risk of premature onset of illnesses, including diabetes and heart disease (Ezzat *et al*., 2012; Lobstein and Jackson-Leach, 2006; Azza *et al*., 2011). Avoiding childhood obesity is the main target to prevent non-communicable diseases and its psychological effects in children and adults and the trans-generational risk of developing obesity.

Macrophage Migration Inhibitory Factor (MIF) is an innate cytokine involved in many inflammatory and autoimmune disorders. It has been implicated as a causal mechanism in a number of disease conditions including cardiovascular and kidney disease (Zernecke *et al*., 2008; Lan, 2008). The MIF is widely expressed in numerous types of tissue and it regulates acute inflammatory as well as adaptive immune reactions (Flaster *et al*., 2007; Cheng *et al*., 2007). Increasing evidence suggests that MIF could control metabolic and inflammatory processes.

Monocyte Chemoattractant Protein-1 (MCP-1) is secreted by macrophages and endothelial cells and is a potent chemotactic factor for monocytes (Yoshimura *et al*., 1989; Deshmane *et al*., 2010). Sartipy and Loskutoff (2003) reported that there was abundance of MCP-1 in both adipose tissue and plasma in obese mice, suggesting that MCP-1 might play an important role in obesity.

Curcumin has a wide range of functions mainly antioxidant; antitumor, anti-inflammatory properties (Anto *et al*., 2002; Lan, 2008; Sandur *et al*., 2007). It could modify various targets involved in obesity and associated metabolic diseases (Ismail *et al*., 2014).

Aim to evaluate to evaluate both serum MPC-1 and MIF in obese subjects and detect the effect of oral curcumin intake.

MATERIAL AND METHODS

The study protocol was approved by the Human Ethics Committee of National Research Centre (NRC), Egypt. Written informed consent was obtained from parent of each child and adult subjects before enrolment. Thirty obese children, defined by BMI >95th percentile for age and sex (Ghalli *et al*., 2008) were enrolment. Also 30 obese adults with BMI >30 were included. They met the following eligibility criteria: age 10-18 years for children and age 20-40 years for adults. Exclusion criteria were acute infection, hypothyroidism and obesity associated with syndromes. Obese subjects suffering from other autoimmune diseases, malignancy or receiving immunosuppressive drugs were also excluded. We divided obese subjects randomly into a trial group and a control group.

The trial subjects received a 500 mg curcumin capsule with the main meal for 4 weeks (Ismail *et al*., 2014). Controls received a placebo capsule for 4 weeks.

Another group of 30 children and 30 adults with normal weight serving as controls for laboratory results. They must be healthy and free from acute infections.

All subjects included in this study were subjected to full history taking, thorough clinical examination, with emphasis on blood pressure measured according to American Heart Association guidelines, anthropometric indices: Body weight measured to the nearest 0.1 kg with a balance scale and height measured to the nearest 0.1 cm. Body Mass Index (BMI) was calculated as weight divided by height squared (kg m^{-2}). Waist Circumference (WC) and hip circumference (HIP C) were measured.

Child body fat (%) = (1.51×BMI)-(0.70×age)-(3.6×gender)+1.4

Adult body fat (%) = (1.20×BMI)+(0.23×age)-(10.8×gender)-5.4

where, female = 0 and male = 1 (Deurenberg *et al*., 1991).

Laboratory measurements: Each subject gave fasting blood samples on days 1 and 29. Blood samples were centrifuged and serum was stored at -80°C.

Routine investigation including CBC, thyroid profile, liver and kidney functions were done.

Evaluation of serum MIF and MCP-1 levels were done by commercially available ELISA kits (MIF: Hangzhou East biopharma Co. Ltd., China, MCP-1: Sun red Biological Technology, China) according to the manufacturer's instructions.

Statistical analysis: Conducted using Statistical Package for Social Science (SPSS) program version 15.0 (Chicago, IL, USA). All numeric variables were expressed as Mean±Standard Deviation (SD). Comparison of different variables in various groups was done using Student t test for normal variable. Pearson's and Spearman's correlation tests (r = correlation coefficient) were used for correlating normal and non-parametric variables, respectively. To assess the effect of oral curcumin vs. placebo, the paired sample t test was used to compare means for normally distributed data. The p-values <0.05 were considered as statistically significant.

RESULTS

The study included 60 obese subjects (30 children and 30 adults). Obese children mean age was 14.71±4.52 years, male/female 9/21. Obese adults mean age was 37.55±9.93 years, male/female11/19. A total of 60 normal wt. enrolled as controls. Thirty children their mean age was12.241±3.11 years, male/female 11/19. Thirty adults their mean age was 34.35±10.75 years, male/female 10/20. Table 1 shows a comparison between obese subjects and controls as regard to anthropometric measurements. We found a significant difference (p = 0.000) between both groups. The mean level of MIF was higher in obese subjects than in controls 7.90±3.88, in children 4.46±1.98 ng mL^{-1} and in adults 7.08±2.45, 5.04±1.93 ng mL^{-1}, p = 0.000. As regard, the mean serum level of MPC-1 it was significantly higher in obese group than in controls. In children the mean value was 21.57±11.10 vs 7.38±4.09 pg mL^{-1}, respectively, p = 0.002. In adults the mean value was 38.20±54.04 vs 9.25±3.53 pg mL^{-1}, respectively, p = 0.018.

The MCP-1 was correlated significantly with BMI, WHTR, percentage body fat and MIF in adults (r = 0.418, 0.292, 0.393, 0.425, respectively and p = (0.001, 0.026, 0.002 and 0.001, respectively). Obese children showed similar correlation (Table 2).

Table 3 shows the results of comparison between curcumin intake group versus placebo group in children and adults. No significant variation was detected between groups.

Trial results are shown in Table 4 and Fig. 1a-b and 2a-b. Curcumin intakes resulted in statistically significant decrease in serum MPC-1 and serum MIF in children and adults. As regard, the placebo group no significant change was observed (Table 5).

Table 1: Comparison between obese children and adults and normal weight controls

Groups	No. of children	Mean	SD	Sig. (2-tailed)	No. of adults	Mean	SD	Sig. (2-tailed)
Age years								
Obese	30	14.7100	4.52	0.050	30	37.5500	9.93	0.219
Normal wt. controls	30	12.2400	3.11		30	34.3500	10.75	
BMI								
Obese	30	33.9700	6.24	0.000	30	37.8000	6.64	0.000
Normal wt. controls	30	22.1200	2.77		30	21.3300	2.55	
WHTR								
Obese	30	0.6300	0.07	0.000	30	0.7500	0.18	0.001
Normal wt. controls	30	0.5000	0.08		30	0.6000	0.16	
Body fat (%)								
Obese	30	40.5200	7.28	0.000	30	44.8400	10.65	0.000
Normal wt. controls	30	24.7000	5.09		30	23.9700	5.85	
MPC-1 (pg mL^{-1})								
Obese	30	21.5700	11.10	0.002	30	38.2071	54.04	0.018
Normal wt. controls	30	7.3800	4.09		30	9.5226	3.53	
MIF (ng mL^{-1})								
Obese	30	7.9000	3.88	0.000	30	7.0800	2.45	0.000
Normal wt. controls	30	4.4667	1.98		30	5.0400	1.93	

Sig: Significant, SD: Standard deviation, BMI: Body mass index, MPC-1: Monocyte chemoattractant protein-1 and MIF-1: Migration inhibitory factor-1

Table 2: Correlation between MPC-1 and MIF with indices of obesity in children and adults

Parameters	BMI	WHTR	PBF	MPC-1	MIF-1
Children					
MPC-1 (pg mL^{-1})					
Correlation coefficient	0.462**	0.454**	0.431**	1.000	0.272*
Sig. (2-tailed)	0.001	0.001	0.002	-	0.046
MIF-1 (ng mL^{-1})					
Correlation	0.391**	0.361**	0.365**	0.272*	1.000
coefficient sig. (2-tailed)	0.004	0.008	0.007	0.046	-
Adults					
MPC-1 (pg mL^{-1})					
Correlation	0.418**	0.292*	0.393**	1.000	0.425**
coefficient sig. (2-tailed)	0.001	0.026	0.002	-	0.001
MIF-1 (ng mL^{-1})					
Correlation	0.758**	0.361**	0.700**	0.425**	1.000
Coefficient sig. (2-tailed)	0.000	0.006	0.000	0.001	-

Sig: Significant, BMI: Body mass index, WHTR: Waist to height ratio, PBF: Percent body fat, MPC-1: Monocyte chemoattractant protein-1 and MIF-1: Migration inhibitory factor-1

Table 3: Comparison between curcumin intake group versus placebo group in children and adults

	Children			Adults		
Groups	Mean	SD	Sig. (2-tailed)	Mean	SD	Sig. (2-tailed)
Age years						
Group of curcumin	15.40	5.380	0.40	36.20	10.37	0.458
Group of placebo	13.96	3.430		39.00	9.61	
BMI						
Group of curcumin	35.24	6.120	0.26	38.47	7.91	0.583
Group of placebo	32.60	6.300		37.08	5.14	
WHTR						
Group of curcumin	0.64	0.070	0.36	0.61	0.15	0.387
Group of placebo	0.62	0.070		0.68	0.06	
Body fat (%)						
Group of curcumin	42.50	7.930	0.13	46.80	10.82	0.313
Group of placebo	38.41	6.100		42.73	10.43	
MPC-1 (pg mL^{-1})						
Group of curcumin	22.42	13.480	0.825	28.69	21.60	0.188
Group of placebo	20.60	19.450		19.74	12.55	
MIF-1 (ng mL^{-1})						
Group of curcumin	9.07	4.500	0.16	7.68	2.52	0.414
Group of placebo	6.65	2.713		6.92	2.37	

BMI: Body mass index, SD: Standard deviation, Sig: Significant, MPC-1: Monocyte chemoattractant protein-1 and MIF-1: Migration inhibitory factor-1

Table 4: Effect of curcumin intake in children and adults

	Children groups			Adults groups		
Paired test	Mean	SD	Sig. (2-tailed)	Mean	SD	Sig. (2-tailed)
First sample						
MPC-1 (pg mL^{-1})	22.42	13.80		29.1000	22.36	
Second sample						
MPC-2 (pg mL^{-1})	9.29	5.00	0.000	15.9286	16.55	0.007
First sample						
MIF-1 (pg mL^{-1})	9.07	4.50		7.6800	2.52	
Second sample						
MIF-2 (ng mL^{-1})	5.19	2.02	0.001	4.2000	1.29	0.000

SD: Standard deviation, Sig: Significance, MPC-1: Monocyte chemoattractant protein-1, MIF-1: Migration inhibitory factor-1 and MIF-2: Migration inhibitory factor-2

Table 5: Effect of placebo intake in children and adults

	Children groups			Adults groups		
Paired test	Mean	SD	Sig. (2-tailed)	Mean	SD	Sig. (2-tailed)
First sample						
MPC-1 (pg mL^{-1})	20.60	19.45		19.74	12.55	
Second sample						
MPC-2 (pg mL^{-1})	19.56	19.70	0.119	20.5	22.10	0.275
First sample						
MIF-1 (ng mL^{-1})	6.65	2.71		6.74	2.36	
Second sample						
MIF-2 (ng mL^{-1})	6.58	2.77	0.664	6.43	2.41	0.413

SD: Standard deviation, Sig: Significance, MPC-2: Monocyte chemoattractant protein-2, MPC-1: Monocyte chemoattractant protein-1, MIF-1: Migration inhibitory factor-1 and MIF-2: Migration inhibitory factor-2

DISCUSSION

Recently, it had been reported that MIF and MPC-1could have a role in the inflammatory process in obesity (Lue *et al*., 2002; Deshmane *et al*., 2010). The work was aiming to evaluate both serum MPC-1 and MIF in obese subjects and detect the effect of oral curcumin intake.

The study showed that both circulating MPC-1 and MIF levels were statistically significantly higher in obese children and adults. Same results reported by other authors

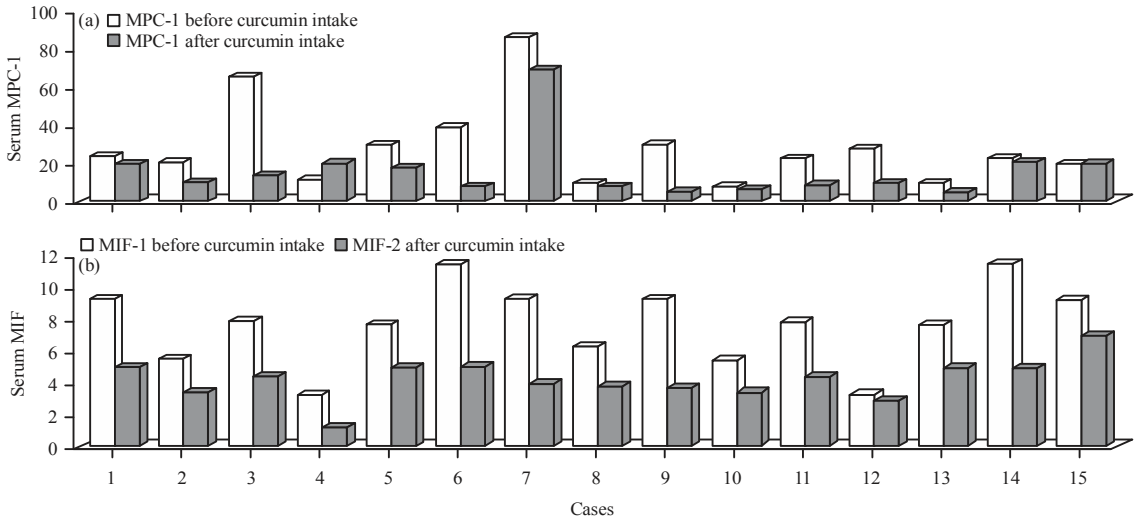

Fig. 1(a-b): Effect of curcumin in adults

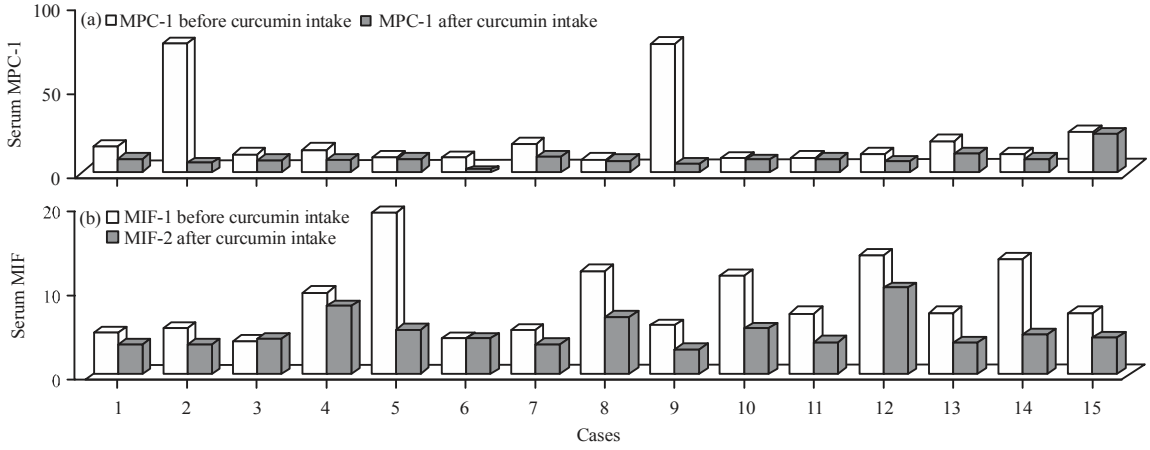

Fig. 2(a-b): Effect of curcumin in children

(Bruun *et al*., 2005). Serum MPC-1 was correlated with indices of obesity as BMI and percentage body fat in all obese subjects. Bruun *et al*. (2005) supported our result and explained it by the fact that MCP-1 is partially produced from the adipocyte fraction which is more in obese subject. Also, Weight loss in obese subjects could to lower serum MIF concentrations.

After curcumin intake obese subjects had significant improvements in serum MIF and MPC-1 levels. Pan *et al*. (2004) reported that increased serum MIF concentrations appear to be associated with β-cell dysfunction. Several vitro studies proved that MIF had a role in glucose metabolism. Benigni *et al*. (2000) found that serum MIF increased catabolism in skeletal muscles. Improvements in MIF may be a sign of improving β-cell function.

The MCP-1 secreted by fat cells especially visceral fat was highly regulated and increased by proinflammatory cytokines and chemokines (Murao *et al*., 1999). Sandur *et al*. (2007) and Ismail *et al*. (2014) supported our result as they found that curcumin has an anti-inflammatory function.

The study has some limitations such as small number of cases and short duration of curcumin intake. Also the study did not evaluate how long this effect persists. Promising result is encouraging to perform a big study for a longer duration.

CONCLUSIONS

Circulating MIF and MPC-1 concentrations were significantly elevated in obese children and adults. Oral intake of curcumin could lower the circulating MIF and MPC-1 levels so it could decrease obesity associated complications.

ACKNOWLEDGMENT

The study was a part of a project supported financially by National Research Centre Fund (NRC) Egypt, grant no. 9090102.

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