

## Original Research Article

# Effect of L-carnitine supplementation on inflammatory marker of coronary artery disease

Abhishek Singhai, Vishal Yadav\*, Rajesh Kumar Jha

Department of Medicine, Sri Aurobindo Medical College & PGI, Indore, Madhya Pradesh, India

**Received:** 21 January 2017

**Revised:** 05 February 2017

**Accepted:** 22 February 2017

### \*Correspondence:

Dr. Vishal Yadav,

E-mail: [doctorvishalyadav@gmail.com](mailto:doctorvishalyadav@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** L-carnitine (LC) might have the potential to control inflammation by reduction of major inflammatory cytokines, including CRP. Therefore, this study was planned to investigate the effect of LC supplementation on CRP levels in CAD patients.

**Methods:** 50 subjects comprised placebo group who received standard line of treatment for coronary artery disease while other 50 subjects comprised LC group who received 1000 mg of LC daily apart from standard treatment for 12 weeks. CRP levels were measured at baseline and again after 12 weeks of treatment in all subjects.

**Results:** The participants in the LC group had significantly lower levels of CRP after 12 weeks of supplementation with LC, than at baseline ( $p < 0.01$ ).

**Conclusions:** We suggest that LC supplementation, due to its antioxidant effects, have potential utility to reduce inflammation in CAD.

**Keywords:** CRP, Coronary artery disease, Inflammation, L-carnitine

## INTRODUCTION

Coronary artery atherosclerosis is the single largest killer of men and women in the United States. It is the principal cause of coronary artery disease (CAD), in which atherosclerotic changes are present within the walls of the coronary arteries. CAD is a progressive disease process that generally begins in childhood and manifests clinically in middle to late adulthood. Initially thought to be a chronic, slowly progressive, degenerative disease, atherosclerosis is a disorder with periods of activity and quiescence. Although a systemic disease, atherosclerosis manifests in a focal manner and affects different organ systems in different patients for reasons that remain unclear. Association between inflammation and atherosclerosis is well established. High levels of

inflammatory markers lead to early development of coronary artery disease (CAD).<sup>1</sup>

C-reactive protein (CRP) is an annular, pentameric protein found in blood plasma, whose levels rise in response to inflammation. It is an acute phase reactant, a protein made by the liver and released into the blood within a few hours after tissue injury, the start of an infection, or other cause of inflammation. Its physiological role is to bind to lysophosphatidylcholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1q complex.<sup>2</sup> The levels of CRP, interleukin-6 and tumour necrosis factor- $\alpha$  were commonly used as markers of inflammation to predict the risk of CAD. Normal concentration OF CRP in healthy

human serum is between 5 and 10 mg/L, increasing with aging. Higher levels are found in late pregnant women, mild inflammation and viral infections (10–40 mg/L), active inflammation, bacterial infection (40–200 mg/L), severe bacterial infections and burns (>200 mg/L).<sup>3</sup>

L-carnitine (LC) might have the potential to control inflammation by reduction of major inflammatory cytokines, including CRP. Therefore, this study was planned to investigate the effect of LC supplementation on CRP levels in CAD patients.

## METHODS

### Study design

This is a prospective study.

### Study setup

This study is conducted at Department of General Medicine of a tertiary care centre.

### Study duration

The duration of study was one year; January-2015 to December-2015.

### Sampling

Purposive sampling technique is used for selection of desired samples according to inclusion criterion.

### Sample size

One thousand patients of general medicine department of a tertiary care centre were evaluated for possible inclusion in study. Out of these 100 subjects were recruited for the study after fulfilling inclusion criteria.

### Inclusion criteria

All adults with coronary artery disease, diagnosed by ECG, Echo or coronary angiography, included in this study.

### Exclusion criteria

Patients with history of diabetes mellitus, hypothyroidism, kidney disease, liver diseases, along with those receiving anticoagulants or high dose of statin therapy were excluded from the study.

### Methods

Demographic characters like age, sex, height, weight of all subjects were noted. Fasting blood glucose (FBG), Lipid profile, serum creatinine, hemoglobin, HbA1c and

TSH estimation done in all subjects. The level of CRP was measured by the enzyme-linked immunosorbent assay method using commercially available kits. 50 subjects comprised placebo group who received standard line of treatment for coronary artery disease while other 50 subjects comprised LC group who received 1000 mg of LC daily apart from standard treatment for 12 weeks. After 12 weeks of treatment, CRP levels were measured again in all subjects.

### Ethical consideration

Prior to conduct of the present study, the protocol of the study was submitted to ethical and scientific committee of hospital. After getting due approval from these two committees, the present study was initiated. Also prior to conduct of study related procedure/investigation, a voluntary written informed consent was taken from the patient /legally acceptable representative.

### Statistical technique

The demographic data of 100 subjects was analysed by statistical software, SPSS version 17.0. Continuous variables were compared with same parameters measured 12 weeks after treatment using two tailed paired t test with a p value of <0.05 being considered as significant.

Financial input and funding: The patient underwent procedures as per protocol laid down by our institution for management of such patients. Hence there was no financial burden on patient or institution. This project was not funded by any of pharmaceutical/diagnostic industry.

## RESULTS

Mean age (SD) of LC group and placebo group was 42.2 (9.8) and 44.6 (10.8) years respectively. The maximum number of subjects in this study was in the age group between 51-60 which was followed by age group of 41-50 and 61-70 respectively. Female preponderance was seen in both groups. Baseline BMI was 26.5 and 25.9 in LC group and placebo group subjects respectively. Serum creatinine was normal in all subjects. Fasting blood sugar level varies from 69-92 mg/dl among LC group subjects. Mean (SD) FBS was 81.74±8.4 mg/dl among LC group subjects. Among placebo group subjects, FBS varied from 82-90 mg/dl. Mean (SD) FBS was 84.28±3.1 mg/dl among placebo group subjects. There were no significant difference in mean cholesterol, HDL, LDL, HbA1c and TSH among placebo and LC group subjects (Table 1).

C Reactive protein levels before and after LC supplementations are shown in Table 2. The participants in the LC group had significantly lower levels of CRP after 12 weeks of supplementation with LC, than at baseline (p<0.01).

**Table 1: Demographic characteristics of all subjects.**

	Placebo group (n=50)	LC group (n=50)	P value
Mean age (SD)	44.6 (10.8) years	42.2 (9.8) years	p>0.05
Sex (female %)	54%	52%	p>0.05
BMI (Kg/m <sup>2</sup> )	25.9	26.5	p>0.05
FBS (mg/dl)	84.28± 3.1	81.74±8.4	p>0.05
Serum creatinine (mg/dl)	0.8±0.1	0.9±0.1	p>0.05
Serum HDL (mg/dl)	36.4±11.9	39.6±10.8	p>0.05
Serum LDL (mg/dl)	119±12.3	121±11.8	p>0.05
HbA1c	6.3±0.4	6.2±0.3	p>0.05
Serum TSH	4.1±2.1	3.8±2.9	p>0.05

**Table 2: Levels of CRP before and after LC supplementation.**

	Placebo (n=50) Mean±SD	LC (n=50) Mean±SD	P value
<b>Week 0</b>			
CRP (mg/L)	2.3±3.2	2.3±3.3	0.58
<b>Week 12</b>			
CRP (mg/L)	2.7±3.3	1.1±1.1	<0.05

## DISCUSSION

The word atherosclerosis is of Greek origin and literally means focal accumulation of lipid (i.e. athero [gruel]) and thickening of arterial intima (i.e. sclerosis [hardening]). Atherosclerosis is a disease of large and medium-sized muscular arteries and is characterized by endothelial dysfunction, vascular inflammation and buildup of lipids, cholesterol, calcium, and cellular debris within the intima of the vessel wall. A major advance in the treatment of coronary artery atherosclerosis has been the development of a refined understanding of the nature of atherosclerotic plaque and the phenomenon of plaque rupture, which is the predominant cause of acute coronary syndrome. Atherosclerotic plaques (or atheromas), which may require 10-15 years for full development, characteristically occur in regions of branching and marked curvature at areas of geometric irregularity and where blood undergoes sudden changes in velocity and direction of flow. Decreased shear stress and turbulence may promote atherogenesis at these important sites within the coronary arteries, the major branches of the thoracic and abdominal aorta, and the large conduit vessels of the lower extremities.

CRP was so named because it was first identified as a substance in the serum of patients with acute inflammation that reacted with the somatic 'C' carbohydrate antigen of *Pneumococcus*.<sup>4</sup>

Discovered by Tillet and Francis in 1930, it was initially thought that CRP might be a pathogenic secretion since it was elevated in a variety of illnesses, including cancer.<sup>5</sup>

The later discovery of hepatic synthesis demonstrated that it is a native protein.<sup>6</sup>

It was demonstrated that LC at a dose of 1000 mg/day significantly reduced inflammation markers in CAD patients. In a similar study by Lee et al on 20 CAD patients with high CRP, showed significant decrease in CRP after LC treatment.<sup>7</sup> They also demonstrated decrease in other inflammatory markers like IL-6, TNF- $\alpha$  also with LC treatment.

Gulcin L studied the antioxidant activity of L-carnitine in vitro. At the concentrations of 15, 30 and 45 mcg/mL, L-carnitine showed 94.6%, 95.4% and 97.1% inhibition on lipid peroxidation of linoleic acid emulsion, respectively. On the other hand, 45 mcg/mL of standard antioxidant such as alpha-tocopherol and trolox indicated an inhibition of 88.8% and 86.2% on peroxidation of linoleic acid emulsion, respectively. In addition, L-carnitine had an effective superoxide anion radical scavenging, hydrogen peroxide scavenging, total reducing power and metal chelating on ferrous ions activities. Also, those various antioxidant activities were compared to alpha-tocopherol and trolox as references antioxidants.<sup>8</sup> Several reports involving about 2500 patients of CAD where L-carnitine was administered for upto 1 year indicate some beneficial effects.<sup>9</sup> There is reduction in ischemia showing reduced ST-segment depression and angina, greater effort tolerance and decreased need of cardiac drugs. L-Carnitine can cause overall improvement in cardiac performance in patients with CAD as well as in cardiomyopathy.

## CONCLUSION

From the present study it was suggested that LC supplementation, due to its antioxidant effects, have potential utility to reduce inflammation in CAD.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the institutional ethics committee*

## REFERENCES

1. Danesh J, Wheeler JG, Hirschfield GM, Eda S, Eiriksdottir G, Rumley A, et al. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. *New England J Medicine*. 2004;350:1387-97.
2. Thompson D, Pepys MB, Wood SP. The physiological structure of human C-reactive protein and its complex with phosphocholine. *Structure*. 1999;7:169-77.
3. Clyne B, Olshaker JS. The C-reactive protein. *J Emergency Medicine*. 1999;17:1019-25.
4. Ananthanarayan R, Paniker C. Ananthanarayan and Paniker's Textbook of Microbiology (7th ed.): Orient Longman. p. 218. ISBN 9788125028086.
5. Tillett WS, Francis T. Serological reactions in pneumonia with a nonprotein somatic fraction of pneumococcus. *J Experimental Medicine*. 1930;52:561-71.
6. Kennelly PJ, Murray RF, Rodwell VW, Botham KM. *Harper's illustrated biochemistry* 2009. McGraw-Hill Medical. ISBN 0-07-162591-7.
7. Lee BJ, Lin JS, Lin YC, Lin PT. Anti-inflammatory effects of L-carnitine supplementation (1000 mg/d) in coronary artery disease patients. *Nutrition*. 2015;31:475-9.
8. Gülçin L. Antioxidant and antiradical activities of L-carnitine. *Life Sci*. 2006;78(8):803-11.
9. Singh RB, Aslam M. L-carnitine administration in coronary artery disease and cardiomyopathy. *J Assoc Physicians India*. 1998;46(9):801-5.

**Cite this article as:** Singhai A, Yadav V, Jha RK. Effect of L-carnitine supplementation on inflammatory marker of coronary artery disease. *Int J Adv Med* 2017;4:467-70.