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Research Article

Effect of dietary lycopene on inflammatory marker in patients of heart failure

Asutosh Prafulchandra Chauhan*, Pankil K. Shah

Department of Biochemistry, GMERS Medical College, Gotri, Vadodara, Gujarat, India

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***Correspondence:**
Dr. Asutosh Prafulchandra Chauhan,
E-mail: dr.ashutoshchauhan@gmail.com

ABSTRACT

Background: Heart failure (HF), often referred to as chronic heart failure (CHF), occurs when the heart is unable to pump sufficiently to maintain blood flow to meet the body's needs. Patients with HF are characterized by systemic inflammation, as evident by raised circulating levels of several inflammatory cytokines with increasing levels according to the degree of disease severity. Inflammation occurs in the vasculature as a response to injury, lipid peroxidation, and perhaps infection. Inflammation can be a significant contributor in the pathophysiology of HF. Antioxidants may slow the progression of HF because of their ability to inhibit damaging inflammatory processes. The purpose of this study was to test a dietary intervention in patients with HF to assess the effect of dietary lycopene on biomarkers of inflammation.
Methods: Sixty participants with HF were randomly assigned to 1 of 2 groups: lycopene intervention and non-intervention. The lycopene intervention group received 27.212 mg of lycopene intake per day by drinking 1 serving (243 gm) of tomato soup for 30 days. We obtained serum lycopene, and C-reactive protein (CRP), to determine the impact of the intervention.
Results: Plasma lycopene levels increased in the intervention group compared with the usual group (0.50 µmol/L to 0.75 µmol/L, P = 0.002; 0.55 µmol/L to 0.57 µmol/L). C-reactive protein levels decreased significantly in the intervention group in both women and men. The pre-intervention and post-intervention CRP level for women was 15.37 ± 1.46 mg/dL and 8.32 ± 1.11 mg/dl respectively and for men was 15.05 ± 2.58 mg/dL and 8.14 ± 1.49 mg/dL respectively.
Conclusions: These findings suggest that the antioxidants in a 30-day intervention of tomato soup significantly decreases CRP levels in a sample of female and male patients with HF.

Keywords: Heart failure, Inflammatory biomarkers, CRP, Lycopene

INTRODUCTION

Although enormous progress has been made in the prevention and treatment of cardiovascular disease (CVD), it remains the leading cause of death throughout the Western world and the second most common cause worldwide.[1] By the year 2020, it is estimated that nearly 40% of all deaths worldwide will be due to CVD, more than twice the percentage of deaths from cancer

Heart failure is commonly a result of ischemic heart disease or hypertension. Inflammation plays a role in all stages of atherothrombosis, the underlying cause of approximately 80% of all Sudden Cardiac Death (SCD). The connection between increased antioxidant intake and reduced cardiovascular disease (CVD) risk has been demonstrated in epidemiologic and observational studies.[2-5] Heart failure has a major inflammatory component, and ischemic CVD is the most common

cause of HF.[6] The connection between inflammatory pathways and disease progression of HF has been supported by studies reporting elevated plasma cytokine levels found in patients in various stages of HF.[7]

The oxidative stress originates mainly in mitochondria from Reactive Oxygen and Reactive Nitrogen Species (ROS/RNS) and can be identified in most of the key steps in the pathophysiology of atherosclerosis and the consequential clinical manifestations of cardiovascular disease. In addition to the formation of atherosclerosis, it involves lipid metabolism, plaque rupture, thrombosis, myocardial injury, apoptosis, fibrosis and failure. The recognition of the critical importance of oxidative stress has led to the enthusiastic use of antioxidants in the treatment and prevention of heart disease.[8] Role of antioxidants in reducing the inflammatory process have been indicated.[9-11] Reactive oxygen and nitrogen species in high levels in the plasma is thought to be one of the contributing factors to CVD because of the oxidation of lipids and damage to the endothelium of the vasculature.[12-15] Increased amounts of reactive oxygen species in the myocardium can be caused by increased inflammatory cytokines or by an impairment of antioxidant production. Increased antioxidant plasma levels established in connection with fruit and vegetable intake have been found both to be inversely related to HF incidence and to demonstrate a lower risk of events related to HF.[16,17] Lycopene is a superior antioxidant found in raw and processed food products and is considered to be one of the most efficient antioxidant at reducing reactive oxygen species, also known as free radicals.[18,19] Oxidative stress occurs when there is a state of imbalance between free radicals and endogenous antioxidants.[14] Given the role of inflammation in HF, a novel strategy for preventing or delaying the complications of HF may be to increase lycopene intake in the diet.

Thus, the purpose of this randomized controlled study was to test the effect of an intervention of a lycopene present in food product on biomarkers of inflammation in patients with HF. Our first objective was to compare the serum levels of C-reactive protein (CRP) in 2 groups of patients with HF. The first group (intervention) consumed 1 serving of tomato soup, daily and was compared with a second group (control) of HF patients who did not consume tomato soup daily.

METHODS

The study population

Sixty patients having etiology of heart failure were selected from IPD and OPD departments. They were randomly divided into two groups either an intervention group (n=40) or a control group (n=20). The intervention group was given one serving (243 gm) of fresh tomato soup to drink each day for 30 days while consuming their normal diet. The control group continued to consume their normal diet and no tomato soup was given to them. Data collection included clinical information, random 24-hour dietary food recalls, and blood samples for levels of CRP, and lycopene.

Sample collection and preparation

Eligibility criteria for patients in this study included (1) confirmed diagnosis of HF, (2) hospitalized for HF within the last 6 months. *Exclusion criteria:* (1) younger than 25 years; (2) having end-stage renal disease, a co morbidity with a known inflammatory component, or a disease. (3) Having illness that was predicted to cause death. No patients were lost to follow-up during the 1-month time frame. The final sample size of intervention group was 40 patients (21 men and 19 women).

Measurement

Plasma lycopene was obtained into purple EDTA vacutainer tubes from venous blood (approximately 5 mL) that was drawn via needle and syringe from the forearm. Plasma was immediately separated from red blood cells by centrifuging at for 10 minutes. Blood plasma was then placed into vials and stored at -80C and sent to laboratory with facility of lycopene estimation where extraction and HPLC-Photo diode array analysis was carried out.

C-reactive protein: C-reactive protein was measured by CRP-latex slide agglutination test. Latex particles coated with goat IgG anti-human CRP are agglutinated when mixed with samples containing CRP. Sample dilutions with saline 1:2, 1:4…. 1:64 were prepared and tested according to the qualitative procedure until no further agglutination was observed. The CRP concentration was then estimated from last dilution with visible agglutination and by turbidometric assay.

Dietary intake assessment

Dietary nutrient intake was assessed using a 24-hour diet recall method to determine (1) free living intake of lycopene and (2) sodium intake, as processed foods containing lycopene are often high in sodium. Serving size estimation charts were provided to assist with accuracy in conducting dietary recalls. These data were collected at baseline and then randomly once a week for 3 weeks, for a total of 4 recalls for each patient.

RESULTS

A total of 60 patients who were all categorized as NYHA class II or III were selected. Most of the patients had an ischemic HF etiology. There were no significant differences between patients in the control group or the intervention group with respect to age, gender, body mass index (BMI), HF etiology, NYHA classification, medications, and smoking history or exercise patterns. All patients who enrolled in study completed the study.

Statistical analysis**:** All data analyses were conducted, and a P value of <0.05 was considered statistically significant. To compare baseline differences between the 2 treatment groups, paired and unpaired t tests were used.

Serum lycopene levels increased significantly in intervention group as compared to control group.

Table 1: S. lycopene in control and interventional group.

S. lycopene	Control group	Intervention group
At start the study	0.55 µmol/L	0.50 µmol/L
After the study (30 days after)	0.57 µmol/L	0.75 µmol/L

P value - 0.002

S. CRP: Serum level of CRP considerably decreased in all the intervention subjects irrespective of gender.

Table 2: S. CRP in male.

S. CRP	Pre intervention	Post intervention
Mean	15.05 mg/dl	8.14 mg/dl
SD	2.58 mg/dl	1.49 mg/dl

t-16.6987, P value <0.0001

Table 3: S. CRP in female.

S. CRP	Pre intervention	Post intervention
Mean	15.37 mg/dl	8.32 mg/dl
SD	1.46 mg/dl	1.14 mg/dl

t-18.6425, P value <0.0001

DISCUSSION

This is the study in which an intervention of a lycopene-rich food source has been tested in a sample of patients with HF. To date, there have been 2 other studies in which the role of antioxidants in patients with HF has been studied. In both studies, there was a positive association between plasma lycopene levels and HF; both of these studies were observational.[20,21] In our study, we found a significant effect of lycopene intervention on the levels of CRP, a potential inflammatory marker. Another pilot study done on this topic showed gender effect on the CRP level showing that lycopene intervention decreased CRP level significantly in women but not in men.[22] But in our study there was no gender difference observed. There was, however, no evidence in our sample that women were more compliant to the intervention than men were. Lycopene levels increased significantly in both genders in the intervention group over time, while remaining unchanged in both genders in the control group. Interleukin-6 enhances liver production of CRP. Levels of inflammatory markers in obese persons (BMI Q30 kg/m2) are considered independent predictors of CVD. Higher Waist-to-Hip Ratio (WHR) and greater waist circumference have been found to be independently associated with a significantly increased age adjusted risk of CVD and HF.[23-25] In the Nurses' Health Study, women with a WHR of 0.88 or higher had a relative risk of 3.25 (95% confidence interval, 1.78-5.95) for CVD compared with women with a WHR of less than 0.72.[23] There was no gender difference in BMI level in our sample of patients. However, we did not measure abdominal adiposity. This additional measurement may have shed additional light onto our findings. Often, the effect of a variety of interventions (e.g., cardiac rehabilitation, weight loss, intake of healthy foods) is greater in those in whom the outcome of interest is most negatively affected. That is, those who have the most to gain(or lose)often show the largest effect of an intervention, at least initially.[26-28] There is sufficient evidence to support that CRP plays a direct role ininflammation.[29] The fact that our study found that CRP levels decreased in response to a dietary intervention is a positive finding. Any decrease in CRP levels, such as the one observed in our study, has the ability to reduce the risk of further cardiac events and is considered to be of important value to clinicians and patients.[30,31] C-reactive protein levels have also been shown to predict mortality in patients with dilated cardiomyopathy and to have an inverse association with left ventricular function in patients with HF.[32,33] If CRP levels are increased in patients with HF, they will further increase with the severity of the pathology and be associated with a higher rate of mortality independently of any ischemic cause.[33,34] Our data also indicate that increased consumption of lycopene-containing food products results in increased plasma levels of lycopene. These data support previous studies where increased dietary intake of lycopene is reflected in increased circulating lycopene levels in plasma.[35-37] Compliance to the tomato soup intervention was observed in both women and men in our study. Processed foods containing high levels of lycopene also contain high levels of sodium and high sodium intake is an independent risk factor for HF exacerbation.[38-40] Our study tested a randomized intervention on top of evidence based drug regimens for patients with HF and found an impact of a dietary intervention. We cannot attribute the intervention effect solely to lycopene, as tomato soup does contain a variety of antioxidants and vitamins in small amounts. However, it does contain a large amount of lycopene. With regard to the feasibility of this study of a dietary intervention, we found that patients with HF were able to adhere to the intervention, as evidenced by a compliance rate of 100%. The patients did not report any ill effects from drinking the lycopene product for 30 days. This intervention was easily implemented by a sample of patients with difficult self-care regimens. In addition to establishing feasibility, the study has strength in the 2-group randomization of participants. There are several limitations to this study. Because of the small sample size, it is difficult to generalize to the entire population of people with HF. Additional biomarkers of inflammation, such as inflammatory cytokines, could be measured in conjunction with CRP to further elucidate the impact of inflammation in HF.

CONCLUSION

The study of the role of dietary antioxidants as interventions for inflammation in patients with HF is novel. Lycopene is a natural plant compound found in fruits and vegetables. Lycopene containing products are inexpensive, readily available. In a sample of patients with HF who received a lycopene-rich dietary product, we found a significant increase in plasma lycopene levels. Serum CRP levels, as a biomarker of inflammation, did decrease in the intervention group as a whole. These findings suggest that the naturally occurring antioxidant lycopene interacts to affect CRP levels in a sample of patients with HF. Although a physiologic mechanism is unclear, additional studies will help clarify this finding. This study provides insight to the potential role of antioxidants, such as lycopene, in HF and may lead to additional treatment strategies. These findings are a preliminary step in a process of establishing efficacy of a specific dietary intervention with antioxidants that may have a clinically significant effect on inflammation in patients with HF.

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