

Higher Levels of Serum Lycopene are Associated with Reduced Prevalence and Mortality of Metabolic Syndrome

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Article Information

Received date: Jul 26, 2016

Accepted date: Jul 27, 2016

Published date: Aug 05, 2016

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Metabolic syndrome is a cluster of metabolic disorders, including increased fasting glucose, blood pressures, plasma triglyceride, and reduced High-Density Lipoprotein (HDL) cholesterol concentrations and abdominal obesity [1]. According to the National Cholesterol Education Program's Adult Treatment Panel III, to be diagnosed with metabolic syndrome, an individual has to meet three or more of the following criteria: 1) abdominal obesity (waist circumference >40 inches for men and >35 inches for women); 2) hypertriglyceridemia (serum triglyceride ≥ 1.69 mmol/L); 3) low HDL-cholesterol (HDL <1.04 mmol/L for men and <1.29 for women); 4) hypertension ($\geq 130/85$ mmHg) and 5) high fasting glucose (fasting glucose ≥ 6.1 mmol/L) [2]. Metabolic syndrome is common among overweight and obese individuals, and leads to an increased risk of cardiovascular disease and type 2 diabetes mellitus [1, 2]. Although the mechanisms behind metabolic syndrome are not entirely clear, accumulating evidence supports that chronic inflammation and oxidative stress play important roles in its development [3, 4].

There have been a number of different strategies or interventions intended to mitigate the oxidative stress and/or inflammation. One is the therapeutic drug strategy. For example, salsa late, a traditional anti-inflammatory medication, can prevent the metabolic syndrome in obese non-diabetic individuals [5]. Probuco, a potent anti-oxidant drug, has been in clinical use during the past few decades for prevention of cardiovascular diseases [6]. While these therapeutic drug strategies that target weight-related oxidative stress and/or inflammation can potentially reduce chronic disease burdens, often these anti-oxidants and anti-inflammatory drugs have serious side effects in long-term disease prevention. For example, approximately 30% of patients discontinued use of salsa late because of gastrointestinal symptoms and tinnitus [7] and many patients discontinued use of probuconol because of QT interval prolongation [8].

A diet rich in antioxidants is another potential approach to reduce oxidation and inflammation. Nutrient intake from food, such as lycopene, may be an ideal option for long-term disease prevention. As an antioxidant, lycopene is mainly contained in tomatoes and other vegetables or fruits, such as red carrots and watermelons. The biological mechanisms of lycopene on metabolic syndrome include alleviating oxidative stress and inhibiting inflammation in the body [9-13]. Studies found there is a significant association between metabolic syndrome and lycopene [14-16]. For example, Sluijs et al, found that higher lycopene intake is associated with a lower prevalence of metabolic syndrome in middle-aged and elderly men [14]. Liu et al. found that higher serum lycopene levels were associated with a lower prevalence of metabolic syndrome in middle-aged and elderly Chinese adults [15]. Yeo et al. also found there is a significantly positive association between metabolic syndrome and serum lycopene among Korean men [16].

Despite accumulating evidence to support health effects of lycopene, it is not clear whether lycopene has similar effects among individuals who are overweight or obese. Many recent studies on lycopene have focused on people who are overweight or obese [17-22]; however, the results remain inconclusive. For example, some studies found that lycopene intervention can significantly reduce inflammation and oxidative stress in participants who are overweight and obese [17-20], while other studies did not find significant associations between lycopene and inflammation and oxidative stress in overweight or obese individuals [21, 22].

One of the potential reasons for varying effects of lycopene is differences in the amount of serum lycopene in these studies. Two cell culture studies found a dose-dependent relationship between the serum lycopene concentration and the amount of reduction in inflammation and oxidative stress [23, 24]. These findings explain non-significant results of lycopene studies when the serum concentration was notably lower. Another point to consider when interpreting the research findings on lycopene is variations in the level of oxidation and inflammation in different individuals. By definition, compared to normal weight individuals, overweight and obese individuals should have

higher levels of oxidation and inflammation. It is possible that among overweight and obese individuals with already high oxidation and inflammation levels, a substantially larger amount of lycopene needs to be applied in order to have observable changes. Our previous results clearly indicated that with the equal level of serum lycopene, the effects of serum lycopene on the prevalence of the metabolic syndrome are only significant for participants who are normal weight or overweight, but not significant for participants who are obese [25]. Furthermore, the findings of our study also indicated that a high level of serum lycopene could have significant health effects among adults regardless of their BMI levels [unpublished results].

In addition to be associated with reduced prevalence of metabolic syndrome, higher levels of serum lycopene are associated with reduced mortality in individuals with metabolic syndrome [26]. Alleviating oxidative stress and decreasing inflammation may also be an alternative explanation for reduced the risk of mortality by lycopene in individuals with metabolic syndrome. In summary, higher levels of serum lycopene are associated with reduced prevalence and mortality of metabolic syndrome. However, due to being cross-sectional studies, further prospective studies need to verify the association between serum lycopene and the prevalence and mortality of metabolic syndrome.

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