Commentary

Interventional Cardiology

Astaxanthin for heart failure: a friend or foe?

Takao Kato[1], Ryo Naito[1,2*], Takatoshi Kasai[1,3]

[1]Department of Cardiovascular Biology and Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan
[2]Cardiovascular Respiratory Sleep Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan
[3]Sleep and Sleep-Disordered Breathing Center, Juntendo University Hospital, Tokyo, Japan

*Author for correspondence:
E-mail: rnaitou@juntendo.ac.jp
Received date: August 01, 2020
Accepted date: August 14, 2020
Published date: August 21, 2020

Commentary

The prognosis of heart failure is still poor despite advances in the treatment of heart failure, such as evidence-based medical therapies, improvement in cardiac device therapies, and endorsement of healthy behaviors [1].

Oxidative stress has been established in the etiology of cardiovascular disease, a precursor of heart failure (HF), and worsens the progression of HF via enhanced reactive oxygen species (ROS) production, reduced antioxidant reserve, and ROS-mediated cardiac injury [2,3]. However, antioxidant therapies have not been demonstrated as effective treatments for HF. For example, 1-month vitamin C therapy had no effect on exercise capacity and even worsened skeletal muscle metabolism in patients with HF [4]. Similarly, vitamin E administered to diabetic or atherosclerotic patients showed no preventive effects on the incidence of HF; instead, it increased HF-related hospitalizations [5]. A meta-analysis showed that high-dose vitamin E was, in fact, associated with an increased risk of all-cause mortality [6].

Astaxanthin is a carotenoid widely distributed in nature, especially in deep red-colored natural sea products such as salmon, salmon roe, shrimp, and crabs [7]. Astaxanthin exhibits high antioxidative properties and its strong antioxidant effect is 1.6 times that of lycopene, 5 times that of β-carotene, 1000 times that of vitamin E, and 6000 times that of vitamin C [8,9]. As humans cannot synthesize carotenoids, astaxanthin is only acquired and accumulated through the diet.

Recently, we conducted a pilot study on the effects of astaxanthin in HF patients (10). The study included 16 adult HF patients with reduced left ventricular ejection fraction (LVEF), who had New York Heart Association functional class ≥ II and were under treatment with standard medical therapies. A commercially available astaxanthin supplement containing 12 mg of astaxanthin, 40 mg of tocotrienol, and 30 mg of L-ascorbic acid 2-glucoside (AstaReal ACT, AstaReal Co., Ltd., Tokyo, Japan) was administered to the patients. Our study showed that 3-month astaxanthin supplementation improved LVEF with an increase of 11.4 % (from 34.1 % at baseline to 38.0% at 3 months, p=0.03) and extended 6-minute walking distance by 39.4 meters (from 393.4 meters to 432.8 meters, p=0.02), with a concurrent decrease in mean reactive oxygen metabolite (dROM) (from 385.6 Carratelli unit to 346.5 Carratelli unit, p=0.04). Increase in LVEF was significantly related to decrease in dROM (r=-0.692, p= 0.003). This is the first study to demonstrate that astaxanthin confers beneficial effects on cardiac function and exercise tolerance in HF patients with reduced LVEF.

There has been conflicting evidence on the health benefits of astaxanthin. Previous experimental studies using animal models have reported that astaxanthin attenuated exercise-induced oxidative stress in the heart and reduced myocardial fibrosis following myocardial infarction [11-13]. Additionally, positive effects of astaxanthin on skeletal muscles were reported from a randomized controlled study demonstrating improvement in exercise performance among competitive cyclists [14]. The beneficial

effects of astaxanthin on the heart and skeletal muscles could be explained by its antioxidative and anti-inflammatory properties as indicated by previous findings of reduction in the markers of oxidative stress and inflammation in healthy individuals [15-17]. Besides that, the inhibitory property of astaxanthin against oxidative stress-related mitochondrial dysfunction may constitute another beneficial effect [18].

However, we cannot yet confirm the beneficial effects of astaxanthin in HF patients until further studies corroborate our findings and address the following issues raised by previous studies. First, randomized controlled studies have not yet been conducted in HF patients; hence, the causality between astaxanthin and its effects on cardiac function and exercise tolerance cannot be confirmed. Second, multiple comparisons for multiple outcomes in our study could generate chance results. Thus, double-blind randomized placebo-controlled trials with adequate sample sizes and primary outcomes on changes in cardiac function or exercise capacity and pre-specified secondary outcomes should be conducted. Further, the astaxanthin supplementation used in our study contained not only 12 mg of astaxanthin but also 40 mg of tocotrienol and 30 mg of L-ascorbic acid 2-glucoside. Since the latter compounds also have antioxidative properties, they could potentially contribute to improvement in cardiac function and exercise tolerance, assuming that the beneficial effects are yielded via mitigating oxidative stress.

Astaxanthin has the potential to improve cardiac function and exercise tolerance in HF patients possibly through mitigating oxidative stress, inhibiting inflammation, and preventing oxidative stress-related mitochondrial dysfunction. Further studies are needed to unravel the mechanisms linking astaxanthin to its health benefits.

Funding

This study was supported by JSPS KAKENHI (Grant Number, 18K15904). This funding source played no other roles in this study.

References

1. Savarese G, Lund LH. Global public health burden of heart failure. Card Fail Rev. 3(1): 7-11 (2017)
2. van der Pol A, van Gilst WH, Voors AA, et al. Treating oxidative stress in heart failure: past, present and future. Eur J Heart Fail. 21(4): 425-435 (2019).
3. Mangge H, Becker K, Fuchs D, et al. Antioxidants, inflammation and cardiovascular disease. World J Cardiol. 6(6): 462-477 (2014)
4. Nightingale AK, Crilley JG, Pegge NC, et al. Chronic oral ascorbic acid therapy worsens skeletal muscle metabolism in patients with chronic heart failure. Eur J Heart Fail. 9(3): 287-291 (2007).
5. Lonn E, Bosch J, Yusuf S, et al. Effects of long-term vitamin E supplementation on cardiovascular events and cancer: a randomized controlled trial. JAMA. 293(11): 1338-1347 (2005).
6. Miller ER, Pastor-Barriuso R, Dalal D, et al. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. Ann Intern Med. 142(1): 37-46 (2005).
7. Hussein G, Sankawa U, Goto H, et al. Astaxanthin, a carotenoid with potential in human health and nutrition. J Nat Prod. 69(3): 443-449 (2006).
8. Miki W. Biological functions and activities of animal carotenoids. Pure & Appl. Chem. 63(1): 141-146 (1991).
9. Nishida Y, Yamashita E, Miki W. Quenching Activities of Common Hydrophilic and Lipophilic Antioxidants against Singlet Oxygen Using Chemiluminescence Detection System. Carotenoid Science. 11: 16-20 (2007).
10. Kato T, Kasai T, Sato A, et al. Effects of 3-Month Astaxanthin Supplementation on Cardiac Function in Heart Failure Patients with Left Ventricular Systolic Dysfunction-A Pilot Study. Nutrients. 12(6): 1896 (2020).
11. Aoi W, Naito Y, Sakuma K, et al. Astaxanthin limits exercise-induced skeletal and cardiac muscle damage in mice. Antioxid Redox Signal. 5(1): 139-144 (2003).
12. Gross GJ, Lockwood SF. Cardioprotection and myocardial salvage by a disodium disuccinate astaxanthin derivative (Cardax TM). Life Sciences. 75(2): 215-224 (2004).
13. Zhang J, Wang QZ, Zhao SH, et al. Astaxanthin attenuated pressure overload-induced cardiac dysfunction and myocardial fibrosis: Partially by activating SIRT1. Biochim Biophys Acta Gen Subj. 1861(7): 1715-1728 (2017).
14. Earnest CP, Lupo M, White KM, et al. Effect of astaxanthin on cycling time trial performance. Int J Sports Med. 32(11): 882-888 (2011).
15. Park JS, Chyun JH, Kim YK, et al. Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans. Nutr Metab (Lond). 7(18) (2010).
16. Fassett RG, Coombes JS. Astaxanthin in Cardiovascular Health and Disease. Molecules. 17(2): 2030-2048 (2012).
17. Fassett RG, Coombes JS. Astaxanthin: a potential therapeutic agent in cardiovascular disease. Mar Drugs. 9(3): 447-465 (2011).
18. Wolf AM, Asoh S, Hiranuma H, et al. Astaxanthin protects mitochondrial redox state and functional integrity against oxidative stress. J Nutr Biochem. 21(5): 381-389 (2010).