Relationship between zinc and heart disease

- Otoniel Santiago
- Shanil Juma, PhD

Cardiovascular disease (CVD) is the number one common cause of morbidity and death in all ethnicities. There are many contributing factors associated to this disease, which include: atherosclerosis, type 2 diabetes, high cholesterol, lack of physical activity and obesity [1-3] . Despite the many studies performed in these areas, nutrition and nutritional status play a major role in the decrease of CVD. One area that has been look at for almost a decade is the relationship of micronutrients in preventing the onset of cardiovascular disease. Although there are still many controversies in the areas of diet and obesity, the role of micronutrients especially zinc, have been closely studied to identify if its levels have any effect in reducing or potentially inducing cardiovascular disease. The purpose of this report will be to briefly discuss how zinc levels may play a role in promoting cardiovascular disease or preventing it.

Zinc Functions

Zinc is known as one of the essential trace elements vital for maintaining normal physiology and cellular functions in the body. [1] It was during the 1960's that zinc deficiency was discovered after it was found that dwarfism and delayed sexual maturation were related to zinc. This discovery lead to an increase in clinical studies in order to understand the critical role of zinc in human physiological growth and its relation to other conditions such as, dermatitis, impaired taste, and impaired immunity to name a few. [1] Nonetheless, the role of zinc is not completely understood. This trace

element has only been known for the past 50 years, but it has been clearly documented that it can improve an array of conditions like acute diarrhea in children, the common cold, and reduction of oxidative stress, the making of genetic material and wound healing. In all, zinc plays a major role in protein synthesis, thus, making it one of the most essential micronutrient needed for optimal health in the human body.

Zinc and Heart Disease

Zinc has been known for its many protective capacities and functions. However, low zinc levels have been associated with age, disease and lack of nutritional intake. It has been found that zinc deficiency increases the inflammatory response caused by increased vascular oxidative stress. [2] For instance, in patients with type 2 diabetes suffering from cardiovascular disease, it was found that zinc serum levels were low [3] . Despite the fact that low serum zinc levels were found to be an independent factor for heart disease in patients with type 2 diabetes, non-diabetic patients who suffered from CVD was related to lower consumption of zinc. [3]

Zinc deficiency can also be associated to malabsorption caused by gastric conditions such as Chron’s disease and celiac sprue, or conditions like diabetes which increase zinc loss due excessive urinary output [4.] A study conducted by Frustaci et al, looked at selenium and zinc deficiency to identify if cardiac malfunction could occur with individuals who suffer from intestinal malabsorption. The study found that there was a great association of between the deficiency of selenium and zinc and the degeneration of

cardiomyocytes [5] . Although this study looked into two micronutrients, it is important to point out that zinc played a major role in this study. As mentioned previously, zinc is an essential trace element that works in nearly over 300 enzymes exerting catalytic, structural, and regulatory functions [4, 5] . In addition to these functions, a deficiency of zinc can cause cell apoptosis and necrosis due to its role in growth and development.

On the other hand, selenium has been associated with the Keshan disease that causes progressive dilated cardiomyopathy [5] . Both elements serve as antioxidants detoxifying cardiomyocytes from free radicals and a deficiency of any of these two elements can cause a decline a cardiac function [5] . Patients in this study were treated with a selenium/zinc infusion of 13. 6 mg/d/wk for about six months. The group was divided into two groups consisting of one group of (A2, n= 8) and another (A1, n= 10). [5] All patients in group A1 received cardiac catherization, and an endomyocardial biopsy, while the A2 group were only treated with anti-heart failure therapy. Nonetheless, after the six months was completed group A1 showed an improvement in their left ventricle dimension when compared to the A2 group who only received supportive therapy [5] . The study determined that a selenium and zinc cardiomyopathy can occur in patients with intestinal malabsorption and that an infusion of both elements can improve and possibly prevent the malabsorption associated cardiomyopathy [5] .

In another study conducted by Soinio et al, after a seven year period follow up on both non-diabetic patients and type 2 diabetic patients, it was found that there was an increase in mortality from CVD in patients with lower

serum levels of zinc (≤14. 1µmol/l) then those who did not (14. 1> µmol/l) [3] . Most patients on this study were between the ages of 45-64 and the population consisted of 1, 050 patients from West and East Finland where 526 were men and 470 were women. Each participant was examined for zinc serum levels after a 12hr fast. Zinc serum levels were determined through atomic absorption spectrotometry after 10 years from stored samples. Out of the 1, 050 participants 156 died of coronary heart disease and 254 patients suffered a myocardial infarction.

The rest of the surviving participants were divided in groups of non-insulin treated and insulin treated subjects. Those with insulin treatment had a 15. 3 µmol/l of fasting serum zinc levels when compared to the non-insulin treatment that had 15. 8 µmol/l fasting serum zinc levels. However, after breaking the result into quartiles the results were that low serum levels were an independent risk factor for coronary heart disease for coronary heart disease and fatal/non-fatal myocardial infarctions in patients with type 2 diabetes [3] . Nonetheless, most of the lower serum zinc levels found in diabetics was related to urinary zinc excretion when compared to non-diabetics. It is important to point out that zinc play critical role in the synthesis and function of insulin and the inhibition of pathways that can lead to apoptosis and possibly the upregulation caspase genes [3] .

In this study zinc was added to in vitro insulin preparations to extend the time of insulin action. Despite insulin being added to the treatment of 149 of the participants with type 2 diabetes, serum zinc levels had no considerable changes between the two groups. Thus, there is a possibility that zinc

supplementation may be useful to prevent atherosclerotic complications in type 2 diabetes individuals [3] .

Another study showed that coronary artery disease was more prevalent among individuals with diabetes [4] . In the same study patients with coronary artery disease had higher urinary excretion of zinc when compared to those without coronary artery disease. In addition there was no association with the zinc levels and diseased arteries, but there was an increase in urinary zinc loss and the number of diseases arteries [4] . In relation to diabetes mellitus similar to the study performed by Soinio et al, patients with diabetes excreted greater amounts of zinc when compared to normoglycemic individuals [4] . Regardless of the zinc loss linked to diabetes mellitus and polyuria, zinc concentration was not associated with the onset of coronary arterial disease. The loss of zinc, on the other hand, correlated to the severity of the coronary artery disease. Consequently, the loss of zinc causes a shift of zinc from the intracellular fluid to the extracellular fluid to maintain homeostasis. Thus, affecting zinc dependent enzymes such as the activating nuclear factor Ä¸B and the reduction of nitric oxide bioavailability and the macrophage-mediated oxidative modification of LDL cholesterol along with the inflammatory cascades associated with it that ultimately promote atherogenesis [4] .

On the other hand, zinc only accounts for about 0. 1% of total body pool and zinc plasma concentrations are an insensitive marker for whole body reserves. Thus, the use of the urine zinc/24hour ratio is a better marker to reflect the risk of coronary artery disease. This was compared to other

studies that identified that children from parents with coronary artery disease had higher zinc urinary levels. Suggesting that genetically predisposed children with coronary artery disease have in a long term, ongoing zinc losses taking place before the manifestations of clinical symptoms [4] . Yet, the question still remains whether supplementation of zinc in individuals with low zinc serum levels could prove to be beneficial to prevent or eliminate cardio arterial disease.

In relation to children Sadoh looked if there was any relationship in loss of serum zinc levels with congenital heart diseases and pneumonia. Sadoh looked at 41 Nigerian children with confirmed congenital heart disease and 41 without congenital heart disease. Because congenital heart diseases with left or right shunt are associated with pulmonary over-circulation, which leads to congestive heart failure, the loss of serum zinc levels seem to be increased with pneumonia [6] . In addition, it has been shown that patients with heart failure who are also receiving diuretic therapy are prone to develop zincuria. The medications associated with zincuria are thiadize and angiostenin converting enzyme inhibitors.

In poor countries like Nigeria, children are forced to live with chronic heart failure and the bronchopneumonia, which as mentioned previously can cause low zinc levels. Another possibility for these children to have low zinc serum levels can be related to poor food intake and absorption that arises from the malnutrition they are exposed to [6] . All participants were evaluated for congenital heart disease and any febrile conditions that would had altered

results. In any case, patients would have had to resolve the febrile condition prior to the commencement of the study.

Patients were seen every month for seven months were 3 ml of blood was collected from each person. Serum zinc levels were evaluated using the Dogan et al method and atomic absorption spectrophotometer [6] . The results showed that the mean zinc levels in children congenital heart disease was 101. 3± 21. 6 µg/dl when compared to the controlled who had 106. 5 ± 18. 3 µg/dl. In children less than one years of age, the mean serum zinc was the highest at 102. 6 ± 30. 7 µg/dl when compared to children ten years and older at the lowest levels 94. 8 ± 12. 4 µg/dl. Sadoh also compared children with bronchopneumonia whose zinc levels were lower 89. 5 ± 15. 0 µg/dl indicating an increase loss of zinc due to the disease. When compared to children without bronchopneumonia, the zinc levels were at 103. 9 ± 22. 2 µg/dl [6] .

This study showed that congenital heart failure along with complications such as bronchopneumonia increases the chances of low zinc serum levels. Zinc plays a major role as an acute phase reactant in bronchopneumonia thus, causing its depletion in children with both of these conditions. Whether the patients with severe pneumonia usually have low zinc serum levels, the combination of both pneumonia and congenital heart disease make patients more susceptible to low zinc levels. The same is applied to patients with chronic congenital heart disease, although their levels seem to be lower due to the use of diuretics as a treatment. In all cyanotic congenital heart disease patients had higher levels of zinc when compared to those with acyanotic

congenital heart disease [6] . In this study no zinc supplementation was used, but it can be safe to say that a supplementation could have resulted in improvement of both conditions as seen in the previous studies.

Conclusion

Zinc appears to have protective effects in coronary artery disease and cardiomyopathy in individuals suffering from type 2 diabetes and children with congenital hearts diseases. Intracellular zinc plays a critical role in the oxidative stress reduction protecting from the inflammatory response caused atherosclerosis, type 2 diabetes, and other diseases. Zinc supplementation has been shown to improve cardiac function and prevent further damage. Thus, its investigation, although emerging in the cardiovascular disease research, its mechanism needs to be better understood in order for it to be used as a preventative and treatment of cardiovascular disease.

References

1. Little PJ, Bhattacharya R, Moreyra AE, Korichneva IL. “ Zinc and Cardiovascular Disease.” *Nutrition* 26. 11/12 (2010): 1050-057.
2. Abdel-Khalek Abdel-Salam N, Wessam Aly W, Ahmed Hamza S, Mosfata Fahmy H, Kamel Mortagy A. Relation between zinc level and one year mortality among elderly patients with heart failure. Egyptian J H Med. 2014; 54: 11-14.
3. Soinio M, Marniemi J, Laakso M, Pyörälä M, Lehto S, Rönnemaa T. Serum zinc level and coronary heart disease events in patients with type 2 diabetes. *Diabetes Care.* 30: 523-528, 2007.

4. Giannoglou G, Konstantinou D, Kovatsi L, Chatzizisis Y, Mikhailidis D. Association of Reduced Zinc Status With Angiographically Severe Coronary Atherosclerosis: A Pilot Study. Angiology. July 2010; 61(5): 449-455.
5. Frustaci A, Sabbioni E, Fortaner S, Farina S, del Torchio R, Tafani M, Morgante E, Ciriolo MR, Russo MA, Chimenti C. Selenium- and zinc-deficient cardiomyopathy in human intestinal malabsorption: preliminary results of selenium/zinc infusion. *European Journal Of Heart Failure.* February 2012; 14(2): 202-210 .
6. Sadoh WE, Sadoh AE. Serum zinc values in children with congenital heart disease. *African Health Sciences.* September 2013; 13(3): 601-606.