Effects of Nutrition on Sickle Cell Crises

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Abstract

Background: Sickle cell anemia is one of the most prevalent hereditary disorders in the world, resulting in morbidity and mortality. However, there are recent studies that clearly demonstrate that antioxidants and other supplements can reduce the occurrence of symptoms and cause improvement in health in people with sickle cell disease.

Results: In majority of the patients in the studies reviewed, there has been a decrease in sickle cell crises through nutrition.

Discussion: The numerous studies should interest more practitioners in using nutrition to treat sickle cell disease patients.

Conclusion: These studies suggest that there is a significant effect of nutritional supplementation on sickle RBCs. Natural health care should be evaluated as a potential agent to reduce complications of sickle cell anemia.

Background

Sickle disease is an inherited disorder that affects hemoglobin, the molecule in red blood cells that delivers oxygen to cells throughout the body. People with this disease have red blood cells that contain an atypical type of hemoglobin molecule called hemoglobin S. This atypical molecule causes red blood cells to change into a crescent shape, making it difficult for them to pass through small blood vessels. The sickle shaped cells often block the small blood vessels, which causes less blood to reach that area of the body. The adhesive tendency of these cells causes pain episodes in the arms, legs and abdomen, and the lack of blood flow from blood vessels to tissues results in lung tissue death. When red blood cells become sickled, they break down prematurely, which typically leads to anemia. Anemia causes symptoms like fatigue, shortness of breath, and delayed growth and development in children. It also causes damage to most organs including the kidneys, spleen, liver, and brain. Damage to the spleen makes sickle cell patients easily overwhelmed by certain bacterial infections. Another complication of sickle cell disease is high blood pressure in the blood vessels that supply the lungs resulting in pulmonary hypertension, which occurs in one-third of adults with sickle cell disease and can lead to cerebral vascular disease(1,2).

In sickle cell disease patients, there is a certain population of erythrocytes that have an elevated density. Case reports by Ohnishi (6) found that a cause for the formation of dense cells included calcium-activated potassium efflux and concomitant dehydration. This increase in density is believed to induce the painful crisis of patients with sickle cell anemia. The increased density adds to the sickle cells' difficulty of transporting through the capillary vessels causing them to block arteries. These events lead to an anemic and painful condition. The deoxygenation-oxygenation cycling causes the sickle cell to stretch because of damage cause by free radicals to the sickle cell's membrane. It has been theorized that if the cell membrane was given nutrients to protect itself against free radicals, sickling could be reduced. Ohnishi (7) did find that plasma containing the antioxidants inhibited dense cell formation of the sickle cells. These nutrients provided a stabilization of the cell membrane during the deoxy-oxy cycling of erythrocytes, preventing the dehydration of cell, and halting the leaking of calcium-ions, inhibiting the activation of the calcium-activated potassium efflux channel and the formation of dense cells. By maintaining the cell membrane, the density of the cell decreases, resulting in a decrease in the formation of crescent cells. This reversible process would lead to a decrease in the incidence of sickle cell crisis.

Sickle cell anemia affects millions of people throughout the world. It is most common among people who ancestors come from Africa, Mediterranean countries such as Greece, Turkey, and Italy; Spanish speaking countries (Central America, Cuba, South America); India, and Saudi Arabia. In the United States, sickle cell disease is the most common inherited blood disorder in the United States, affecting 70,000 to 80,000 Americans. The disease is estimated to occur in 1 in 500 African Americans and 1 in 1,000 to 1,400 Hispanic Americans(3,4).

Sickle Cell anemia is similar to thalassemia, a group of inherited disorders which affect the production of hemoglobin causing anemia. They both cause paleness, shortness of breath, spleen enlargement, and fatigue. They are both genetic disorders in the people of the Mediterranean and African descent. The difference involves how they cause the similar symptoms. Thalassemia differs from sickle cell anemia in that there's no abnormal shape of the affected cells, but rather a decrease in the amount of hemoglobin produced causing anemia(5).

The relationship between the occurrences of symptoms and nutrition is becoming more visible in the eyes of doctors across the globe. More doctors are becoming more interested in the health benefits of optimal nutrition and vitamin therapy. Sickle cell anemia and sickle cell trait are genetic disorders and cannot be cured. However, there are recent studies that clearly demonstrate that antioxidants and other supplements can reduce the occurrence of symptoms and cause improvement in health in people with sickle cell disease.

Sources and selection criteria

This review is based on information from published research studies. Electronic searches were done through Pubmed and Medline. There were 150 articles found related to sickle

cell anemia and nutrition. 25 of those articles contained relevant studies on the effects of diet and supplementation on sickle cell anemia.

Results

Aged Garlic Extract

There were numerous studies done antioxidants on sickle cell patients. One shows the result of a density gradient configuration in which concentrations of aged garlic extract (AGE) were added to blood suspension and incubated for 30 minutes before the depolarization oxidation cycle. The study showed a decrease in the amount of dense cells after the AGE was added to blood obtained from sickle cell patients. There were inhibitory effects of 0.6mmol/L Calcium, 0.05mmol/L Vitamin E, and 20mmol/L of NaCN. All results showed inhibitory effects on dense cell formation(6,7). Without the addition of aged garlic extract, the sickled cells would become dense once they came into contact with oxygen. These dense cells would eventually block the arteries and lead to a crisis. However, adding aged garlic extract 30 minutes prior to oxygen contact decreased the amount of develop dense cells.

Two studies related the amount of Heinz body formation to aged garlic extract. He and other scientists theorized that dense sickle cell formation was related to the production of Heinz bodies formed through oxidation. They explained the instability of hemoglobin in sickle cells resulted in a higher amount of free radical generation inside the cells. This process lead to the formation of the Heinz bodies that damage the sickle cell's membrane. This lead to the investigation of data that supports significant anti-oxidant activity of AGE, and its affects on decreasing Heinz body formation. Their research lead to a study which five patients (two men and three women, mean age 40+15 years, range 24-58 years) with sickle cell anemia were given aged garlic extract. AGE was administered at a dose of 5ml a day for 4 weeks. The results showed no significant changes in red blood cell count, hemoglobin level, hematocrit, or reticulocye count. However, in all patients, the generated Heinz body count decreased from 58.9 to 29.0 percent.

Magnesium

By increasing erythrocyte Mg content in sickle cell patient, studies show that there is a decrease in erythrocyte dehydration. Erythrocyte dehydration is caused by the activity of the erythrocyte potassium chloride co-transport and a decrease in cell potassium content. Magnesium is an important regulator of ion transport across the cellular membrane. With this in mind, the supplementation of Mg in sickle cells might cause a decrease in the activity of K-Cl co-transport thus hydrating the cells and increasing their density. A study was conducted involving 10 patients who received O.6 meq/kg/d Mg over a period of six weeks. The results showed a decrease in the amount of erythrocyte K content. Erythrocyte K-Cl co-transport was also reduced significantly. This reaction caused a reduction in the number of dense sickle cells(14). Other studies show a reduced erythrocyte Mg content in sickle cells compared to normal blood. Patients were given oral Mg supplements for 14 to 28 days during the study. A significant increase in Mg content was observed after the 14 to 28 day supplementation(8). Other observations

included a reduction in the K-Cl, Na-K, and Na-K-Cl co-transport activities. K-Cl co-transport activity decline at day 14 and then further decreased at day 28. Significant changes were also observed with Na-K in the maximal rate. No significant reduction or changes were observed in the maximal rate in Na-K-Cl(9).

L-Arginine

Recent studies found that oral L-arginine reduces the incidence of pulmonary hypertension in sickle cell anemia patients. Pulmonary hypertension is a life threatening complication with the list of symptoms of sickle cell disease. This is due to the lack of nitric oxide production, which aids in lowering pulmonary artery pressures in both adults and infants. L-Aginine is a nitrogen donor for the synthesis of nitric oxide. However, during the sickle cell crises there are decreased amounts of L-arginine present in the blood stream. Researchers correlated this with a deficiency in nitric oxide during a sickle cell crises. Ten sickle cell patients were treated with a oral L-argine at a dose of 0.1g/kg three times a day first 5 days. Echocardiographs were given before and after the treatment period of L-arginine on days 0 and 6 and at a 1 month after the completion of L-arginine therapy. Blood samples were drawn a day 0, 3, 6 of the study. Cardiologist were involved in the interpretation of the cardiographs, but were unaware of the therapy. Outcome measurements show a significant reduction of pulmonary artery pressure by an average 15.2% after 5 days of therapy. Only one patient was found to have no significant change through the administration of L-argine therapy. Follow-ups were obtained after 1 month with nine patients with mixed result. Only the patient with no significant changes after the first 5 day was lost due to noncompliance. Four patients exhibited significant improvement. However, four patients reverted back to their previous baseline of pulmonary artery systolic pressure, and one patient demonstrated a worsening of pulmonary arterial pressure(10).

Vitamin E

In a study involving vitamin E therapy, 6 patients had an average of 25 percent of irreversible sickle cells prior to treatment. A-tocopherol and lipid levels were measured before administering the therapy. Patients were given 450 IU of vitamin E three times daily. There were blood samples taken periodically and tocopherol levels were examined. The percentage of circulating irreversibly sickled red cells decreased from 25 % pretreatment to 11% after vitamin E administration. The percentage of irreversibly sickled red cells remained below pretreatment levels as long as the vitamin was administered, up to 35 weeks(11).

Natta and Machlin related most irreversibly sickled cells to a vitamin E -deficiency. When a sickle cell becomes dehydrated or when its hemoglobin gives off oxygen, the hemoglobin polymerizes causing the cell to form a crescent shape. However once the sickle cell becomes oxygenated some of them go back to that normal red blood cell shape. The irreversible sickle cells refer to those cells containing the hemoglobin S that still show a crescent shape even when re-oxygenated. Vitamin E is an antioxidant when is activated in the body is referred to as a-tocopherol. Vitamin E intercepts free radicals therefore preventing lipid destruction chain reactions. Vitamin E maintains the integrity

of cell membranes, is essential for the maintenance of the heart, and sex organs. It has been reported that most sickle cell anemia patients show low plasma levels of vitamin E(12). In the present study, they observed profound decreases in the number of circulating irreversible sickle cells in sickle cell anemia patients when given 450 IU of vitamin E(13).

Thiocyanate

In 1932 Torrance and Schnabel discovered that thiocyanate relieved the entire sickle cell crisis(19). Cyanate, an inhibitor of sickling, forms from the oxidation of thiocyanate, which is formed from nitrilosides in food plants. In the tropical areas of Africa, the average African diet may include large amounts of thiocyanate-yielding foods like cassava, sorghum, and millet grains. Just consuming one kilogram of these foods daily could provide native Africans with one gram or more of thiocyanate. According to Rockefeller University clinical trial of cyanate, this dosage is twice the amount of thiocyanate successfully used to relieve the sickle cell crisis(14).

In comparison, the American diet lacks significant sources of nitriloside. Only yams would be an exception, but yams are rarely consumed in the typical American diet. Cabbage, among vegetables, provide the highest thiocyanate levels. Milk may provide 2 to 8 mg/quart. If the African American community generally consumed one-half pound of cabbage a day and drank 1 quart of milk/day, he or she would only obtain 25 mg thiocyanate from his daily diet. That is only one fortieth the amount an African intakes regularly. This difference in the amount of thiocyanate correlates with the incidence of sickle cell anemia in African and America. Sickle cell anemia occurs in 1 of 50 sicklers in the United states, while only 1 of 1,000 sicklers in Africa. From the evidence it is suggested that sickle cell anemia results from a nutritional deficiency(19).

Discussion

Based on these studies, there should be more use of nutritional supplements in the treatment of sickle cell crises. These studies point out the significant deficiencies of antioxidants and other nutrients in sickle cells patients. If sickle cell crises are a result of dehydration in cells, the reasonable solution would be to find out what stops the cells from dehydrating. Researchers found out that certain nutrients like Mg, aged garlic extract, and vitamin E helped maintain the integrity of sickle cells and therefore avoid cell dehydration and increased density. Research found fewer sickle cell attacks in patients on these supplements. The findings suggest cheaper alternative methods to medicine, and replenishing only what seems to be lacking. How can we deny the possibility of reducing the occurrences of pain episodes among sickle cell patients? Supplements such as vitamin E and garlic which help prevents the efflux of cellular fluid and halt cell deformity. Mg and thiocyanate aid in reversible the cell deformity.
The results of these studies should lead doctors to investigate treating other symptoms of sickle cell anemia naturally. For example, a study that involves increasing the life expectancy of sickle cell patients. If nutrient therapy can decrease the amount of dense sickle cells, could it increase the life of red blood cells in SCA patients. This would lead

to fewer needed transfusions per year among SCA patients. More research studies on nutritional approaches to this disease should be considered.

Conclusion

These studies suggest that nutritional supplements do have a profound affect on sickle cell crisis as well as other conditions related to this disease. There should be more consideration of nutritional methods which give patients some relief without many side effects. Hopefully with the continuation of these studies, it will awaken more health care professionals to consider these alternatives as reliable source.

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