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Short Communication

Nutritional Deficiencies in Children; Vitamin D, Iron, and Micronutrient Deficiencies in Children with Sickle Cell Anemia

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Abstract

Children with Sickle Cell Anemia (SCA), have various degrees of macro and micronutrient deficiencies largely due to an increase in cell turnover, poor nutritional intake, and absorption changes. These deficiencies, some of which are well studied, may increase SCA severity and hospitalizations and reduce health-related quality of life. Research in understanding, diagnosing, and correcting macro and micronutrient deficiencies in children with SCA remains an integral part of improving disease outcomes and patient care in this vulnerable population.

INTRODUCTION

Children with Sickle Cell Anemia (SCA), have various degrees of macro and micronutrient deficiencies largely due to an increase in cell turnover, poor nutritional intake, and absorption changes. These deficiencies, some of which are well studied, may increase SCA severity and hospitalizations and reduce health-related quality of life. Research in understanding, diagnosing, and correcting macro and micronutrient deficiencies in children with SCA remains an integral part of improving disease outcomes and patient care in this vulnerable population.

Vitamin D deficiency and disordered calcium homeostasis is not uncommon among pediatric patients, however the risk of vitamin D deficiency among those with SCA-SS is about 5 times greater than their non SCA counterparts, adjusted for time of year and age [1,2]. Given its integral role in calcium homeostasis and bone mineralization, a deficiency in vitamin D leaves children with SCA at risk for worsening musculoskeletal health problems. Levels of serum 25-hydroxy vitamin D <20 ng/ml are linked to acute and chronic pain and bone fracture in this population [3]. There is also a significant association between vitamin D levels of <20 ng/ml and the number of ER visits, hospital admissions for pain crisis, and length of stay in children with SCA [4]. As such, vitamin D levels should be tested in this population, and appropriate supplementation given to those who are deficient.

Magnesium (Mg) is a micronutrient which assists in the activation of vitamin D and helps regulate calcium and phosphate homeostasis in influencing growth and bone maintenance. All enzymes that metabolize vitamin D require magnesium, which acts as a cofactor in enzymatic reactions both in the liver and kidneys. Studies have shown magnesium homeostasis is altered in persons with Hemoglobin SS resulting in lower levels of Mg, which have been associated with red blood cell sickling, increased polymerization and vaso-occlusion [5]. More studies are needed however, as there is conflicting data on the association between magnesium supplementation in length of hospital stay, pain scores, and cumulative analgesia use in patients admitted with vaso-occlusive crisis (VOC).

The anemia in children with sickle cell disease is primarily due to hemolysis. This chronic hemolysis along with multiple blood transfusions often leads to increased levels of serum ferritin and elevated bone marrow iron. Exacerbations of anemia may occur when there is a concomitant iron deficiency as a result of poor dietary intake or decreased iron absorption. Thus, routine screening for iron deficiency anemia, with appropriate treatment when indicated, is recommended. Folic acid supplementation (1 milligram daily) is also given to patients with SCA as folate deficiency is seen in all major hemolytic anemias due to high cell turnover and a subsequent increase in erythropoiesis [6].

Anemia in sickle cell not only signals a reduction of red cell mass and oxygen delivery, but also ongoing red cell breakdown. Although anemia is clearly associated with many detrimental outcomes, some research suggests that it may also have an advantage in lowering risks of potential viscosity-related complications [7]. It has been reported that overt iron deficiency can be associated with a marked reduction in the mean corpuscular hemoglobin concentration-S (MCHC-S) thereby decreasing the sickling tendency and the severity of hemolysis as evidenced in blood smears and in a decrease in the levels of serum indirect bilirubin and lactate dehydrogenase [8]. The clinical improvement in SCA following the induction of iron deficient erythropoiesis by repeated phlebotomies or by erythrocytapheresis has also been reported to decrease the number of pain crisis [9].

Children with SCA experience high cellular turnover compounded by oxidative stress on red blood cells which may cause or exacerbate micronutrient deficiencies, including trace elements involved in the anti-oxidation mechanisms, such as zinc, selenium, and magnesium. The pathophysiology of SCA demonstrates oxidative stress due to an imbalance between production and elimination of reactive oxygen species (ROS) and their effect on red blood cells (RBCs) in the body. RBCs are highly sensitive to ROS that cause damage to the cell membrane, ultimately compromising oxygen delivery and leading to cell aging and death [10]. Copper, which is involved in the ROS process, has been shown to be slightly higher in those with SCA than the average pediatric population [11]. It is argued that elevated copper-to-zinc ratio may be a biomarker of sickle cell oxidative stress and associated complications [5]. Zinc is essential for cell proliferation and differentiation, especially for the regulation of DNA synthesis and mitosis. It has been reported that zinc deficiency is significantly associated with an increased number of home pain crises and an increased incidence of hospitalizations for VOC [12]. Monitoring zinc status in children and adolescents with SCA may be important in reducing disease-associated morbidity and infections including VOC [12,13]. Additionally, selenium is directly associated with hemolysis in SCA as reduced levels may impair the body's antioxidant capacity, resulting in higher ROS formation and further exacerbating oxidative stress [14].

Though continued research is needed on the effects of macro and micronutrient deficiencies in those with SCA, we recommend providers completing a thorough diet history to screen and properly identify deficiencies in this patient population. Consultation with a nutritional specialist, if available, may also help provide detailed dietary suggestions and supplementation recommendations. Social determinants of health must also be considered. Screening families for food insecurity is important as it may help identify those with potential nutrition-related social needs [15].

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