

Correlation of Nutritional Status with Some Micronutrients in Children with Ventricular Septal Defect

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ABSTRACT

Introduction: The aim of this study was to explore the association between the BMI Z score and the levels of some selected common nutrients among children under 5 years old with ventricular septal defect (VSD).

Methods: We recruited children under 5 years of age who were diagnosed with VSD from May 2017 to November 2017 at the Children's Hospital of Nanjing Medical University as research subjects to measure their height/length, weight and serum levels of common nutrients. The nutritional status of the selected children was evaluated by the Z-score method.

Results: A total of 146 children under five years old diagnosed with VSD (78 males, 68 females) were recruited. Iron levels were significantly higher among girls than boys. Pearson correlation analysis showed a negative association between VC and the weight for height Z-score (WHZ) ($r=-0.172$, $P=0.039$), and there was a positive correlation between VC and the weight for age Z-score (WAZ) ($r=0.247$, $P=0.003$). A comparison of Z scores >0 and <0 also revealed that the VC level in the WHZ >0 group was significantly higher than in the WHZ <0 group ($P=0.025$). After linear regression analysis with adjusted as age, gender, and pulmonary artery pressure, there was a positive association between WAZ and VC ($P=0.035$).

Conclusion: Our study found that there may be a positive correlation between VC levels and the nutritional status of children with VSD.

Abbreviations: vsd: Ventricular Septal Defect; Whz: Weight for Height Z-Score; Nst: Nutrition Support Team; Haz: Height for Age Z-Score; Waz: Weight for Age Z-Score; Va: Vitamin A; Vb1: Vitamin B1; Vb2: Vitamin B2; Vb6: Vitamin B6; Vb9: Vitamin B9; Vb12: Vitamin B12; Vc: Vitamin C; Vd: Vitamin D; Ve: Vitamin E; Cu: Serum Copper; Zn: Zinc; Ca: Calcium; Mg: Magnesium Fe: Iron; eNOS: Endothelial NO Synthase

Introduction

Congenital heart disease refers to anatomical abnormalities of the heart and large blood vessels during the embryonic development period or abnormal heart and blood vessel function caused by no closure of the channels that should be closed after birth. Current epidemiological data [1] show that congenital heart disease

accounts for approximately 28% of all major congenital anomalies [2]. On the one hand, due to the progress of society, diagnosis and screening methods have been continuously improving, and thus, increasing numbers of children with congenital heart disease are identified at birth; on the other hand, the process of

industrialization and urbanization has changed the environment. Increasing numbers of women have postponed childbearing age, especially in developed countries, leading to a high incidence of congenital abnormalities. The incidence of congenital heart disease is increasing each year, so studies of congenital heart disease are receiving increased attention.

Due to the abnormal hemodynamics caused by congenital heart disease, children with congenital heart disease often suffer from hypoxia, hyperthyroidism, frequent respiratory infections, and poor gastrointestinal absorption [3], and growth retardation and malnutrition are common in children with congenital heart disease. At present, the European Society of Pediatric Gastrointestinal Hepatology Nutrition has called for the establishment of a "nutrition support team (NST)" aimed at scientifically effective nutritional management of hospitalized children and reduction of the prevalence of malnutrition [4]. However, with the trend in younger children with congenital heart disease becoming increasingly obvious [1], the earlier the time for surgery is, the more favorable it is for children to catch up with children of the same age earlier in their growth and development [5]. Therefore, we should focus our attention and intervention on the nutritional status of children with congenital heart disease.

However, clinical interventions for nutrition are mostly focused on carbohydrates and fats that can provide actual calories, and the importance of micronutrients is often overlooked. Although humans need a few vitamins and trace elements, they are the trace organics necessary for maintaining body health. These substances neither provide energy sources in the body nor constitute the raw material of body tissues or participate in the formation of human cells; however, these substances play a crucial role in the growth, metabolism, and development of the human body. Due to a lack of attention to dietary supplements and poor digestive functions such as malabsorption and diarrhea, children with congenital heart disease are at risk of these micronutrient deficiencies. In addition, diuretics are used in children with congenital heart disease. Diuretics excrete water and sodium through the kidneys to improve circulatory function and at the same time, excrete other water-soluble molecules, including potassium, magnesium, and vitamin C [6]. Studies have shown that early identification of abnormalities in micronutrients and immunodeficiency can help reduce the incidence in children after cardiac surgery [7].

It is necessary to carry out studies of the preoperative nutritional status of children with congenital heart disease, especially infants and young children, and investigate the correlations between nutritional status and various common trace elements and vitamins in our country. Studies have shown that the nutritional status of children with cyanotic and noncyanotic congenital heart disease is significantly different: children with noncyanotic congenital heart disease are more prone to malnutrition [8], and the nutritional status of these children and its influencing factors deserve

more attention. Ventricular septal defect is the representative disease type in noncyanotic congenital heart disease. It is the most common clinical congenital heart disease, accounting for approximately 20% of congenital heart disease [9]. Therefore, in order to ensure the representativeness of the research sample and effectively control for confounding, this study selected ventricular septal defect as the research disease. This research will study the preoperative nutritional status, common elements, and vitamin levels of children with ventricular septal defect younger than 5 years of age and explore the relevance between them, so that we can provide preventive measures for preoperative malnutrition and guide postoperative nutritional intervention.

Methods

Population Included

A cross-sectional study was conducted at the Department of Cardiothoracic Surgery of Children's Hospital of Nanjing Medical University from May 2017 to October 2017. This study comprised 146 children younger than 5 years who were diagnosed with ventricular septal defects by echocardiography and excluded children with other congenital malformations or other diseases (including genetic diseases) affecting growth or nutritional status. The study was approved by the Ethical Committee of Children's Hospital of Nanjing Medical University, and informed consent was obtained from the guardian of the children.

Nutrition Evaluation Method

Anthropometric measurements included weight (kilograms) and length (centimeters), and they were performed according to standard World Health Organization (WHO) procedures [10]. The Z-score method provided by the National Health Statistics Center and recommended by the WHO was used as the evaluation standard. The Z-score was calculated according to the formula $Z\text{-score} = (\text{measurement value} - \text{median value of the same-age and same-sex reference standard}) / \text{standard deviation of the reference standard}$, including height for age Z-score (HAZ), weight for age Z-score (WAZ), and weight for height Z-score (WHZ). The latest WHO reference standard in 2006 was selected to calculate the Z value [11].

Vitamins and Elements Measurement

Serum levels of vitamin A (VA), vitamin B1 (VB1), vitamin B2 (VB2), vitamin B6 (VB6), vitamin B9 (VB9), vitamin B12 (VB12), vitamin C (VC), vitamin D (VD), and vitamin E (VE) were measured by a BH5100T Whole Blood Multielement Analyzer. Serum copper (Cu), zinc (Zn), calcium (Ca), magnesium (Mg) and iron (Fe) levels were measured by an LK3000V vitamin detector (Tianjin Lanbiao Electronic Technology Development Co., Ltd.).

Data Analysis

In this study, SPSS 23.0 statistical software was used for statistical analysis, and $P < 0.05$ indicates a significant difference. General information, zinc, iron, magnesium, copper, calcium, VA,

VB1, VB2, VB6, VB9, VB12, VC, VE, and VD levels of male and female children are described with the mean plus standard deviation. Mann-Whitney U tests verified whether there was a significant difference between different genders. Pearson bivariate correlation analysis was used to evaluate the correlation between Z scores (e.g, WHZ, WAZ, HAZ) and Zn, Fe, Mg, Cu, Ca, VA, VB1, VB2, VB6, VB9, VB12, VC, VE, and VD. Z-values WHZ, WAZ, and HAZ were grouped by 0, and we compared the levels of Zn, Fe, Mg, Cu, Ca, VA, VB1, VB2, VB6, VB9, VB12, VC, VE, and VD between groups, verified whether they met normality and used an independent t-test for data that satisfied normality. If the data did not satisfy normality, the Mann-Whitney U test was used. Using logistic regression analysis, the confidence interval level was 95%. After correction for age, gender, and pulmonary artery pressure, the ratios of Z-values WHZ, WAZ, HAZ and zinc, iron, magnesium, copper, calcium, VA, VB1, VB2, VB6, VB9, VB12, VC, VE, and VD were analyzed, and the 95% confidence interval was calculated.

Results

Demographic Characteristics of the Participants

There were 68 females and 78 males; for females, the mean age was 18.75±17.75 months, mean weight was 9.97±5.15 kg, and mean height was 78.16±18.33 cm, and for males, the mean age was 21.33±18.56 months, mean weight was 11.13±5.20 kg, and mean height was 81.46±18.07 cm. The iron levels of females were significantly higher than those of males (male vs female: iron, 415.03±33.80 vs 427.87±38.33, P=0.033) (Table 1). However, no statistically significant differences of other vitamins and trace elements were existing in males and females.

Table 1: General situation between different genders.

	Boy (N=78)	Girl (N=68)	P value
Age (month)	21.33±18.56	18.75±17.75	0.373
Weigh (Kg)	11.13±5.20	9.97±5.15	0.116
Height(cm)	81.46±18.07	78.16±18.33	0.199
Zn	4.12±0.92	4.13±0.84	0.803
Fe	415.03±33.80	427.87±38.33	0.033
Mg	35.13±5.78	35.61±5.60	0.558
Cu	1.38±0.38	1.36±0.46	0.623
Ca	75.50±6.20	75.23±6.85	0.749
VA	0.63±0.36	0.64±0.29	0.376

VB1	49.23±15.39	50.69±13.93	0.366
VB2	526.73±189.25	481.61±225.51	0.181
VB6	20.70±9.62	19.90±7.91	0.984
VB9	10.56±5.23	9.82±4.18	0.531
VB12	387.09±218.60	383.42±210.85	0.899
VC	33.21±8.30	32.03±8.68	0.323
VE	11.38±1.03	11.37±1.22	0.727
VD	81.32±24.22	73.47±26.11	0.196
WHZ	-0.34±1.65	-0.64±1.80	0.425
WAZ	-0.32±1.44	-0.65±1.66	0.280
HAZ	-0.01±1.83	0.22±1.55	0.502

Correlation Analysis of Elements and Vitamins and Z Scores

Pearson correlation analysis (Table 2) showed that there was a significant correlation between VC and WHZ (r=-0.172, P=0.039), and there was also a significant correlation between VC and WAZ (r=0.247, P=0.003). While, no significant correlation was found between Zn, Fe, Mg, Cu, Ca levels and the Z-value scores WHZ, WAZ, and HAZ. A comparison of Z scores >0 and <0 showed that VC levels in the WHZ>0 group were significantly higher than those in the WHZ<0 group (P=0.025), as shown in (Table 3). As a result, we conducted a linear regression after adjusting gender and age and found VC was positively associated with between WAZ. The P value was 0.035, as shown in (Figure 1) and (Table 4).

Table 2: Pearson correlation analysis of some common vitamins and Z scores.

	WHZ		WAZ		HAZ	
	r	P value	r	P value	r	P value
VA	-0.070	0.402	0.024	0.779	0.062	0.457
VB1	-0.012	0.884	-0.012	0.888	-0.009	0.917
VB2	0.009	0.919	-0.031	0.714	-0.052	0.539
VB6	-0.049	0.562	0.029	0.734	0.077	0.360
VB9	-0.27	0.750	0.048	0.569	0.077	0.361
VB12	0.082	0.330	0.078	0.350	0.001	0.992
VC	0.172	0.039	0.247	0.003	0.146	0.081
VE	-0.152	0.070	-0.077	0.360	0.030	0.723
VD	0.111	0.186	0.154	0.066	0.010	0.902

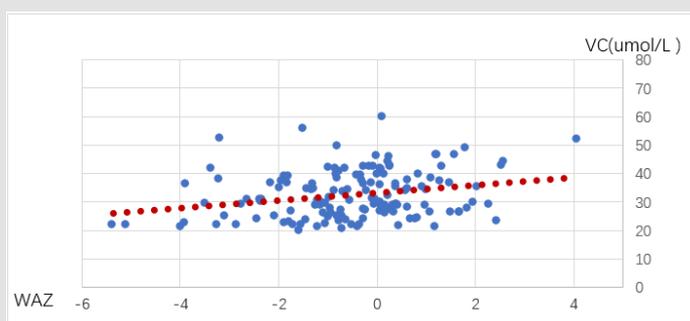


Figure 1: A scatter plot and a fitted line with 95% CI of the relationship between vitamin C and weight for age Z-score in children with ventricular septal defect.

Table 3: Comparative analysis of partial vitamin levels of Z score > 0 group and Z score < 0 group.

	WHZ			WAZ			HAZ		
	<0	>0	P value	<0	>0	P value	<0	>0	P value
VA	0.7±0.4	0.6±0.3	0.561	0.7±0.3	0.6±0.3	0.705	0.6±0.3	0.7±0.4	0.221
VB1	50.6±15.9	48.8±12.8	0.522	50.1±16.0	49.5±12.7	0.968	50.9±15.4	48.8±14.3	0.680
VB2	491.3±215.8	531.2±192.4	0.321	510.6±219.0	503.2±189.0	0.835	506.1±207.2	509.3±207.9	0.804
VB6	20.3±9.0	20.5±8.7	0.596	20.3±9.5	20.4±7.9	0.397	20.8±9.7	20.0±7.9	0.851
VB9	10.4±5.42	10.0±3.7	0.722	10.1±5.2	10.4±4.14	0.343	9.8±3.8	10.7±5.6	0.686
VB12	371.4±212.5	397.3±209.2	0.397	383.3±214.1	379.7±207.7	0.977	379.6±212.4	384.4±210.6	0.870
VC	31.4±8.7	34.1±7.7	0.025	31.4±8.1	34.2±8.5	0.052	31.6±7.7	33.5±8.77	0.180
VE	11.5±1.3	11.2±0.9	0.554	11.5±1.3	11.2±0.9	0.325	11.4±1.2	11.3±0.99	0.826
VD	75.3±25.9	80.8±24.5	0.101	76.2±26.7	79.6±23.4	0.288	78.8±25.3	76.2±25.6	0.633

Table 4: Partial vitamin and Z value regression analysis.

	WHZ		WAZ		HAZ	
	Beta (95%CI)	P value	Beta 95%CI	P value	Beta 95%CI	P value
VA	-0.31(-1.05,0.44)	0.417	0.08(-0.53,0.70)	0.788	0.24(-0.62,1.09)	0.587
VB1	-0.01(-0.02,0.01)	0.570	-0.01(-0.02,0.00)	0.463	-0.01(-0.02,0.12)	0.780
VB2	0.00(-0.01,0.01)	0.586	-0.01(-0.01,0.00)	0.195	-0.01(-0.01,0.00)	0.383
VB6	0.01(-0.02,0.04)	0.663	0.01(-0.02,0.03)	0.597	-0.01(-0.03,0.02)	0.427
VB9	-0.03(-0.08,0.02)	0.233	-0.01(-0.05,0.04)	0.750	0.02(-0.04,0.08)	0.553
VB12	0.01(-0.01,0.01)	0.370	0.00(-0.01,0.01)	0.622	0.00(-0.01,0.01)	0.650
VC	0.02(-0.01,0.05)	0.245	0.03(0.00,0.05)	0.035	0.02(-0.01,0.05)	0.243
VE	-0.08(-0.30,0.14)	0.469	0.05(-0.14,0.22)	0.625	0.10(-0.15,0.35)	0.434
VD	-0.01(-0.02,0.00)	0.272	0.00(-0.01,0.01)	0.460	0.00(-0.02,-0.01)	0.462

Substances are Log10

Corrected gender, age, pulmonary artery pressure.

Discussion

The results of our study revealed a linear regression relationship between VC and WAZ, with a P value of 0.035, suggesting a possible correlation between VC and the nutritional status of children with congenital heart disease. In people with malnutrition caused by chronic diseases, poor eating habits, malabsorption, and other factors, obvious VC deficiency can often be seen [12]. Some animal experiments have shown that VC is an important vitamin for maintaining normal growth and physiological function [13], playing an important role in the growth process [9], collagen formation [14, 15], iron metabolism and hematology [9], reproduction [16], stress response [17], and wound healing [18]. Wang et al. [19]. found that dietary supplementation with VC can significantly increase the daily weight of juvenile ducks. A study by Zhou et al. [20] also showed that increases in body weight, specific growth ratio, protein efficiency ratio, and feed efficiency of VC-deficient fish were lower than those of fish supplemented with VC. In addition, growth performance, antioxidant capacity, and humoral immune parameters of juvenile cobia supplemented with VC were significantly improved [19, 20].

Heart failure increased pulmonary arterial pressure, and anemia are risk factors for protein energy malnutrition in children with congenital heart disease [9], and some physiological functions

of VC can alleviate these risk factors. A considerable amount of research is currently focused on the use of VC to prevent heart failure [21], mainly because of its ability to prevent oxidative damage. Reactive oxygen or nitrogen species (ROS/RNS) are the most common oxidants in the human body and play a key role in aggravating human heart failure [9]. Studies have shown that ROS and RNS can change the properties of lipids, proteins, and nucleic acids, leading to myocardial dysfunction, and myocardial oxidative damage is closely related to congestive heart failure [22]. On the other hand, ascorbate regulates vasodilation by increasing NO synthesis and improving bioavailability [23]. Endothelial NO synthase (eNOS) produces NO, which then diffuses into the smooth muscle cell layer of the vascular wall and causes vasodilation through interaction with soluble guanylate cyclase. Another clinical application of VC is to increase the absorption of nonheme iron [12]. In the small intestine, VC can effectively increase dietary iron transport in intestinal epithelial cells. When anemia patients are supplemented with iron and VC, the synthesis of hemoglobin can be promoted. In addition, studies have also shown [24] that a long-acting VC derivative called ascorbic acid 2-phosphate stimulates cell growth and increases mRNA type III collagen in human osteogenic MG-63 cells and normal human osteoblasts, as well as expression in human bone marrow mesenchymal stem cells, thereby stimulating

proliferation and differentiation of human osteoblast-like cells. In summary, we speculate that VC can indirectly influence the nutritional and growth status of children with congenital heart disease by exerting its biological functions.

VC is mainly related to WAZ, which can reflect acute malnutrition in patients, and we have previously speculated that some trace elements may be related to HAZ, reflecting chronic malnutrition in patients. However, in our research, no correlation was found between Cu, Fe, Zn, Mg, Ca levels and WHZ, WAZ, HAZ; the reasons need further research. Our findings suggest that there is a correlation between VC and WAZ. WAZ is an indicator of acute malnutrition, reflecting the problem of malnutrition at this stage. It is more marked by factors such as disease, feeding method, food choice, and poor nutritional habits [25]. It can be speculated that supplementation with VC can alleviate acute nutritional problems soon.

Conclusion

This study revealed a positive correlation between VC and the nutritional status of children with ventricular septal defects. Further, our results may have implications from the perspective of VC on the nutritional status of children with clinical congenital heart disease intervention, to prevent malnutrition in children before surgery, while guiding clinical staff to carry out postoperative nutritional support in children with congenital heart disease.

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Competing Interests

The authors declare that they have no competing interests.

Compliance with Ethical Standards

Conflict of Interest

The authors have no conflicts of interest to declare.

Ethical Approval

All procedures performed in study were in accordance with the ethical standards of national research committee and with the 1964 Helsinki Declaration and its later amendments.

Informed Consent

Informed consent was obtained from all guardians of patients included in the study.

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