

Correlation Between Serum 25-hydroxyvitamin D3 Levels and Children with Anxiety Disorder

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To cite this article:

Wenjuan Huang, Zhonghong Wang. (2024). Correlation Between Serum 25-hydroxyvitamin D3 Levels and Children with Anxiety Disorder. *American Journal of Clinical and Experimental Medicine*, 12(1), 1-4. <https://doi.org/10.11648/ajcem.20241201.11>

Received: January 6, 2024; Accepted: January 19, 2024; Published: February 1, 2024

Abstract: Objective Explore the correlation between anxiety disorder and serum 25-hydroxyvitamin D3 (25-(OH) D3) level in children, in order to guide the diagnosis and treatment of childhood anxiety disorders and to supply clinical measure. Method The experimental group was 124 children with anxiety disorders attending the Child Behavior and Development Clinic of Jingzhou Maternal and Child Health Hospital from January 2020 to December 2022, as the control group was 131 children who had health checkups in the same hospital during the meantime. The differences of serum 25-(OH) D3 levels between the two groups were compared. Children with anxiety disorder were further divided into 4 age groups according to each group with 2 years (24 months) apart: 11-12 years old (32 cases), 13-14 years old (38 cases), 15-16 years old (31 cases) and larger than 16 years old (23 cases). Then, the difference of 25-hydroxyvitamin D among 16 years old group (23 cases) was compared. Results The serum 25-(OH) D3 level of the experimental group was distinctively lower than that of the control group, [(18.25±7.68) ng/ml VS (28.63±9.52) ng/ml], $P<0.05$, with statistical difference; The rate of vitamin D lack and insufficiency was higher than that of the control group (89.52% VS 75.57%), $P<0.05$, with statistical difference; According to age group grouping, the vitamin D levels in the 15-16 year old and >16 year old groups were lower than those in the 11-12 year old and 13-14 year old groups, with statistically significant differences ($P<0.05$). Conclusion: Vitamin D deficiency is more common in children with anxiety disorders, and is more pronounced in children older than 15 years than in younger children.

Keywords: Anxiety Disorders, 25-hydroxyvitamin D3, Children

1. Introduction

Anxiety disorder in children is one of the more common mental diseases in adolescence. The main clinical manifestations are excessive worry, anxiety, fear and other symptoms, which are diagnosed as "anxiety disorder" in the American Diagnostic and Statistical Manual of Mental Disorders (DSM-V). Existing studies have shown that the anxiety of children and adolescents may have a serious impact on their social adaptability, psychosomatic health and personality formation, and this damage will gradually worsen over time [1, 2]. Anxiety disorder appears in children's adolescence, which may not be conducive to the healthy growth of children and adolescents. This phenomenon has

gradually aroused widespread concern among parents and medical workers. A survey of foreign scholars shows that 11 to 20 percent of children in the United States have behavioral or anxiety disorders [3]. According to the research of domestic scholars, the proportion of children with anxiety was as high as 24.78% when primary school students in a city were surveyed using the screening form for anxiety disorders, of which 5.67% met the diagnostic criteria for children with anxiety disorders. The pathogenesis and etiology of childhood anxiety disorder are still unclear, and some studies have shown that the etiology may be related to social environment, genetics, family education methods, cognition and stress. The purpose of this study was to explore the correlation between vitamin D level and anxiety disorder

in children, and to provide new ideas for auxiliary diagnosis and treatment of anxiety disorder children.

2. Object and Method

2.1. Objects

In this study, 124 children with anxiety disorders, aged 11-16 years old, with an average age of 11.3 ± 2.1 years old, 68 males and 56 females, who were first seen at the Specialized Outpatient Clinic for Child Behavior and Development of Jingzhou Maternal and Child Health Hospital, were selected as the experimental group; The control group consisted of 131 children with health checkups during the same period in our hospital, aged 11-17 years, with a mean age of 11.1 ± 2.4 years, of which 78 were male and 53 were female. The differences in gender and age between the 2 groups were not statistically significant, $P > 0.05$. (Table 1).

Table 1. Clinical data among the two groups.

group	Number of cases	Age (year)	Male/female
Experimental group	124	11.3 ± 2.1	68/56
Control group	131	11.1 ± 2.4	78/53
T/X ²		0.735	0.543
P		0.602	0.596

2.2. Inclusion and Exclusion Criteria

All selected children with anxiety disorder were strictly screened and met the diagnostic criteria of anxiety disorder in children in the tenth edition of the International Classification of Diseases, injuries and causes of death (ICD-10). Exclusion criteria: Children who have had vitamin D supplementation within the last 6 months; Children with generalized developmental disorders, mental disorders caused by epilepsy, schizophrenia, and brain structure abnormalities diagnosed by imaging were excluded.

2.3. Research Methods

Two neurologists specializing in neurology were responsible for taking the history and entering the findings. The Chinese version of the DSM-5 Anxiety Scale for Children and Adolescents is a widely used assessment scale with good reliability in foreign countries. The DSM-5 Child and Adolescent Anxiety Scale is used to assess generalized anxiety symptoms in adolescents and is applicable to children and adolescents 11-17 years of age [4]. The Chinese version of the DSM-5 Anxiety Scale for Children and Adolescents includes 13 questions, each question is scored on a scale of 1-5 (1=none; 2=occasionally; 3=sometimes; 4=often; 5=always), and the total score is Between 13 and 65 minutes. The content of each question indicates the frequency of the adolescent's anxiety symptoms in the previous 1 week. Zhang Youwen and others tested the reliability and validity of DSM-5 anxiety scale for children and adolescents [5].

2.4. 25-hydroxy-vitamin D Detection

3 ml of peripheral venous blood was collected from children with anxiety disorders and healthy children on an empty stomach in the early morning, and serum 25-hydroxy-vitamin D levels were measured using liquid chromatography-tandem mass spectrometry. The VD level was judged by the expert consensus on clinical application of vitamin A and vitamin D in China made by the Child Health Branch of Chinese Preventive Medicine Association and the global consensus on the management of nutritional rickets in 2016: 25-hydroxyvitamin D ≤ 12 ng/L is deficiency; 12 ng/L < 25 -hydroxyvitamin D ≤ 20 ng/L is insufficient; 20 ng/L < 25 -hydroxyvitamin D ≤ 100 ng/L is suitable; 25-hydroxyvitamin D > 100 ng/L is excessive.

2.5. Statistical Methods

statistical analysis: SPSS 22.0 statistical software was used to analyze the data. Count data were expressed as number of cases (%); Measurements are expressed as mean \pm standard deviation; Comparisons between groups were performed using the χ^2 test; The independent samples t test was used to compare the means of the two groups; $P < 0.05$ means the difference is statistically significant.

3. Results

3.1. Comparison of Serum VD Levels Between the Two Groups of Children

The blood collection time of the two groups of children was all in the morning on an empty stomach. The difference was not statistically significant ($P > 0.05$). The serum 25-hydroxyvitamin D level in the healthy control group was higher than that of the children in the anxiety disorder group, and the difference was statistically significant ($t=6.0$, $P < 0.05$). The rate of serum VD deficiency and insufficiency in children in the anxiety disorder group reached (89.52%), which was higher than that in the control group (75.57%), and the difference was statistically significant (table 2).

Table 2. Comparison of serum VD levels between the two groups of children.

group	Number of cases	deficiency	insufficient	sufficient
Experimental group	124	63	48	13
Control group	131	39	60	32
Z			26.153	
P			< 0.05	

3.2. Comparison of Serum 25-hydroxyvitamin D Levels in Children with Anxiety at Different Ages

There were 68 cases of serum 25-hydroxyvitamin D deficiency and deficiency in 15-16 years old group and > 16 years old group. There were 33 cases of serum 25-hydroxyvitamin D deficiency and deficiency in 11-12 years old and 13-14 years old. The proportion of 25-hydroxyvitamin D deficiency and insufficiency in the

elderly group was higher than that in the young group, and the difference was statistically significant ($P < 0.05$) table 3.

Table 3. Level of 25-hydroxyvitamin D of children patients with different ages.

VitD level	Deficiency	Not sufficient	Sufficient
ages			
11-12 years	13	8	5
13-14 years	12	10	4
15-16 years	20	14	2
11-12 years	18	16	2
P values	<0.001	<0.001	< 0.001
F values	554.719	21.945	464.903

4. Discussion

At present, academic circles believe that childhood anxiety disorders are the result of multiple factors such as environmental factors, parenting styles, biology, family history, etc. The specific pathogenesis is still unclear. Most of the existing studies focus on the influence of external factors such as living environment, rearing style, family relationship and their own psychological characteristics, but seldom involve the physiological and biochemical mechanisms that may lead to the occurrence and development of the disease. In recent years, with the advancement of medicine, more and more scholars are studying the neurophysiological mechanisms of anxiety disorders. Existing research certificate that Patients with anxiety disorders have abnormalities in the frontal-temporal page-limbic system pathway, and inappropriate activation of this pathway produces abnormal behavioral, autonomic, and neuroendocrine responses [6, 7]. Secondly, neurotransmitter systems such as 5-hydroxytryptamine, γ -aminobutyric acid, dopamine, and norepinephrine are related to the pathogenesis of anxiety disorders [8].

The important role of vitamin D in bone metabolism has been widely recognized, in addition, it is also involved in cell growth, proliferation, differentiation, apoptosis, membrane transport, immune regulation, oxidative stress, hormone secretion and so on [9]. Recently, vitamin D derivative has been found in cerebrospinal fluid, so it is also considered to be a neurosteroid. It plays an important role in regulating neuronal development and differentiation, antioxidant injury, neurotransmitter synthesis, neurotrophic factor expression and dopaminergic system physiology as well as in the connection and transmission of some neural circuits through the blood-brain barrier [10]. More and more evidences show that cytokines participate in the anxiety process by regulating the metabolism of neurotransmitters such as dopamine and serotonin [10, 11]. Thus, vitamin D may play an important role in children with anxiety disorders.

This study found that the serum VD level of children with anxiety disorders was significantly lower than that of healthy children (18.25 ± 7.68 ng/ml in the experimental group and 28.63 ± 9.52 ng/ml in the control group). Research by domestic scholars shows that children and adolescents have a higher rate of VD deficiency, Shangguan Lili et al. showed

that nearly 30% of children aged 0-7 had VD deficiency or deficiency. A survey of serum vitamin D in preschool children in a city in China found that the vitamin D level of older children was lower than that of younger children, which may be due to the lack of vitamin D supplementation or the reduction of outdoor activities of older children. More and more research reports show that the level of vitamin D in anxiety patients is low [12, 13]. Animal experiments show that vitamin D has obvious anti-anxiety effect on female rats with long-term estrogen deficiency [14]. In addition, studies on patients with anxiety disorders have shown that vitamin D supplementation has a positive effect on reducing anxiety scores [15]. Available clinical evidence suggests that vitamin D deficiency may increase the incidence of autism spectrum disorders, anxiety and depression, schizophrenia, and other disorders, and that vitamin D may play an important role in the development of mental health [16].

5. Conclusions

In summary, serum vitamin D levels in children with anxiety disorders are generally deficient or insufficient, indicating that low levels of VD are important in anxiety disorders, and may be involved in the regulation of neurotransmitters such as dopamine and serotonin, which require further in-depth research. The detection of vitamin D level can be used as an auxiliary examination for children with anxiety disorder, which may provide guidance for the diagnosis and treatment of children with anxiety disorder. There are also limitations to this study: first, there may be an effect of summer and fall and winter and spring on the detection of VD levels; in addition, the sample size of this study was small, and our conclusions can be further substantiated by expanding the sample size.

Abbreviations

VD: Vitamin D

Conflicts of Interest

The authors declare no conflicts of interest.

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