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Low serum levels of 25-hydroxyvitamin D (25-OHD) in children with autism

Baixos níveis séricos de 25-hidroxivitamina D (25-OHD) em crianças com autismo

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Abstract

Objective: To confirm previous evidence suggesting an association between autism and low vitamin D serum levels.

Methods: This preliminary exploratory study assessed the circulating levels of 25-hydroxyvitamin D (25-OHD) in pediatric patients with autism and in typically developing controls from Juiz de Fora, Brazil.

Results: Serum levels of 25-OHD were lower in children with autism (26.48 ± 3.48 ng mL⁻¹) when compared to typically developing subjects (40.52 ± 3.13 ng mL⁻¹) ($p < 0.001$).

Conclusion: Our findings attest to the importance of vitamin supplementation during pregnancy and in the treatment of children with autism, who tend to present low vitamin D consumption rates.

Keywords: Autism, children, vitamin D.

Resumo

Objetivo: Confirmar evidências prévias indicando uma associação entre autismo e baixos níveis séricos de vitamina D.

Métodos: Este estudo preliminar avaliou os níveis circulantes de 25-hidroxivitamina D (25-OHD) em pacientes pediátricos com autismo e em controles apresentando desenvolvimento típico em Juiz de Fora, Brasil.

Resultados: Os níveis séricos de 25-OHD foram menores em crianças com autismo ($26,48 \pm 3,48$ ng mL⁻¹) em comparação com indivíduos com desenvolvimento típico ($40,52 \pm 3,13$ ng mL⁻¹) ($p < 0,001$).

Conclusão: Nossos resultados confirmam a importância da suplementação de vitamina durante a gravidez e no tratamento de crianças com autismo, que costumam apresentar um baixo consumo de vitamina D.

Descritores: Autismo, crianças, vitamina D.

Introduction

Autism is described as a complex neurological condition that undermines normal brain development, leading to conditions such as disturbances in social interaction and communication impairments.¹ Autism spectrum disorders (ASDs) are considered to be caused by different triggers, including nutritional ones.²

In this context, the association between autism and vitamin D levels has been investigated, pointing to possible links between deficient levels of calcitriol [$1,25(\text{OH})_2\text{D}_3$] and some clinical observations^{3,4} – although no single factor can explain why more children are being identified with ASDs. This assumption has been made because this active metabolite plays several important roles: i) inhibition of the synthesis of inducible nitric

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oxide synthase (iNOS), an enzyme responsible for the generation of nitric oxide (NO); ii) modulation of helper T cells, leading to a suppression of autoimmune responses⁵; iii) increase of glutathione levels; and iv) activation of the tyrosine hydroxylase gene expression, increasing the levels of neurotransmitters.⁶ Thus, calcitriol deficiency in early childhood could be in some manner associated with the neurological clinical aspects of autism, and therefore with an increased risk for developing the disorder.⁷

Another suggestion of the importance of vitamin D in the etiology of autism comes from the fact that populations born in environments exposed to reduced levels of UVB radiation, i.e., where vitamin D deficiency is more likely to occur, have higher prevalence rates of this disorder.⁷

Within this context, the present study aimed to conduct a preliminary investigation of the circulating levels of 25-hydroxyvitamin D (25-OHD) in pediatric patients with autism and in typically developing controls from Juiz de Fora, Brazil.

Methods

The study protocol followed the ethical guidelines contained in the Declaration of Helsinki and was approved by the Ethics Committee of Universidade Federal de Juiz de Fora, southeastern Brazil (protocol no. 140/2007). Written informed consent was obtained from the participants' legal guardians.

The sample included 24 children (18 male and 6 female, mean age = 7.4 ± 2.7 years) diagnosed with autistic disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), and also 24 age- and sex-matched healthy controls (18 male and 6 female, average age = 7.2 ± 1.8 years).⁸

Blood samples were collected between 7 and 9 a.m., after an 8-hour fast. Samples were centrifuged at $2465 \times g$ for 10 minutes at $4^\circ C$, and frozen at $-80^\circ C$ for further analysis by high-performance liquid chromatography (HPLC), in duplicate, according to Turpeinen et al.⁹

For statistical analysis, independent samples *t* tests were used to determine numeric group differences. The chi-square test was used to assess binomial data such as sex. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 14.0 (SPSS Inc., Chicago, IL). Two-tailed probabilities of $p < 0.05$ were considered significant.

Results

Among our 24 children with autism, ethnic origin was as follows: males, nine Caucasians and nine non-Caucasians; females, four Caucasians and two non-Caucasians. Among controls, the following numbers were found: males, 15 Caucasians and three non-Caucasians; females, four Caucasians and two non-Caucasians.

With respect to 25-OHD levels according to the sex, no significant differences were observed among children with autism ($p = 0.293$) and among controls ($p = 0.439$). Conversely, serum levels of 25-OHD were significantly lower in children with autism ($26.48 \pm 3.48 \text{ ng mL}^{-1}$) when compared with typically developing subjects ($40.52 \pm 3.13 \text{ ng mL}^{-1}$) ($p < 0.001$). Ethnic differences were not taken into consideration in these analyses.

Discussion

Our results corroborate the previous study by Meguid et al.,⁴ who found $28.5 \pm 16.4 \text{ ng mL}^{-1}$ and $40.1 \pm 11.8 \text{ ng mL}^{-1}$ of 25-OHD in children with autism and typically developing subjects, respectively ($p < 0.001$).

The 25-OHD serum levels found in our sample confirm that children with autism present insufficiency for this vitamin, according to the classification proposed by Holick¹⁰: deficiency, levels $< 20 \text{ ng mL}^{-1}$; insufficiency, levels between 20 and 29 ng mL^{-1} ; and normal, levels $> 30 \text{ ng mL}^{-1}$. Thus, our findings underscore the presence of differences in 25-OHD levels between autistic and typically developing children.

In this light, it is possible to suggest that vitamin D indeed plays a role in normal brain development. Thus, the present findings are useful for clinicians in the sense of calling their attention to the possible need for dietary supplementation with vitamin D during pregnancy and also in the treatment of children with autism and low vitamin D consumption. Notwithstanding, we know that this solely, or any other isolated factor, will not reverse their multifactorial condition.

Further studies are needed in order to confirm the prophylactic potential of vitamin D against ASDs, especially in view of our small sample size. We also suggest the performance of additional assays in the same population, namely serum calcium, parathyroid hormone, phosphate, and bone mineral density.

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