ASSOCIATION OF VITAMIN D DEFICIENCY OR INSUFFICIENCY RICKETS AND AUTISM SPECTRUM DISORDERS, IS IT A HYPOTHESIS OR AN EVIDENCE BASED FACT?

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RESEARCH ARTICLE

ASSOCIATION OF VITAMIN D DEFICIENCY OR INSUFFICIENCY RICKETS AND AUTISM SPECTRUM DISORDERS, IS IT A HYPOTHESIS OR AN EVIDENCE BASED FACT?

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ABSTRACT

There is an agreement among all professionals that autism is one of the most puzzling diseases. It is a complex neurodevelopmental disorder, the prevalence of which has surged in the last 2 decades. Such apparent increase in the prevalence of autism corresponds with the increasing medical advice to avoid the sun, an advice that has probably lowered vitamin D level. Many studies reported low serum concentrations of 25 hydroxy vitamin D in autistics but there were a few reports about autistic manifestations in vitamin D deficiency rickets. This is a commentary about a study that reported a prevalence of 25.71% of mild to moderate autism in a group of Egyptian children with vitamin D deficient or insufficient rickets compared to none of age and sex matched healthy controls and showed a significant negative correlation between the severity of autistic manifestations and serum level of 25 hydroxy vitamin D.

Key words: Vitamin D deficiency, Vitamin D insufficiency, rickets, Autism, Autism Spectrum Disorders (ASDs)

INTRODUCTION

Rickets was first reported in the mid-1600s in Europe. These early reports described typical findings of bone-deformity with curving of the legs. Rickets continued to be reported during successive centuries. By the 1800s, sunlight (ultraviolet radiation) and cod-liver oil were found to be effective in treating rickets, and in the early 1900s, vitamin D was isolated and found to be the essential ingredient of this oil [1]. With the introduction of vitamin D supplementation, rickets became rare in industrialized nations during the 20th century [2].

At the end of the last century, however, two striking things happened. First, nutritional rickets reappeared as an important and widely seen problem in North America. Second, rickets was prevalent in economically-disadvantaged parts of the world where vitamin D deficiency was not properly diagnosed and treated [3].

In spite of improvements in infant mortality and morbidity in many developing countries, nutritional rickets (NR) has been ranked among the 5 most prevalent diseases among children in these countries [4]. In Egyptian infants during their first 2 years of life El-Bishlawy et al., (1992) [5] reported an incidence ranging from 12 to 31.1% of NR. Later, El-Khayat et al., (2006) [6] reported its prevalence to be 29% by screening 1000 Egyptian infants and children aged between 32 and 36 mo who attended the Out-patients’ Clinic, Children's Hospital, Ain Shams University during the period from January to April 2005 for regular follow up or with a mild acute complaint.

On the other hand, autism is usually diagnosed before the age of three years with striking 4:1 male to female ratio [7]. It is characterized by defiance in social reciprocity and in language skills that are associated with repetition behavior and restricted interests [8]. The apparent increase in the prevalence of autism over the last 20 years corresponds with the increasing medical advice to avoid the sun, an advice that has probably lowered vitamin D level. Autism is more common in areas of limited sun exposure such as urban areas and areas of high air pollution. It is also more common in dark skinned persons and in infants exposed to severe maternal vitamin D deficiency in utero. Such epidemiological distribution of autism would theoretically greatly lower activated vitamin D "calcitriol" levels especially in developing brains. Interestingly, some children with vitamin D deficiency rickets were reported to have several autistic markers that apparently disappeared with high dose vitamin D treatment [9].
Because of all foregoing interesting data, Zaky et al., (2015) [10] investigated the prevalence of Autism Spectrum Disorder (ASDs) in an Egyptian sample of vitamin D deficient/insufficient rachitic infants and children compared to age and sex matched healthy controls and correlated the level of 25 hydroxy vitamin D with the severity of autistic manifestations using Childhood Autism Rating Scale (CARS). Thirty five vitamin D deficient/insufficient rachitic Egyptian infants and children (group I) and 35 clinically healthy age and sex matched controls were enrolled (group II). Rickets biochemical markers, 25 hydroxy vitamin D, and Vineland Adaptive Behavioral Scales were assessed for all studied infants and children. DSM IV TR criteria were used for diagnosis of ASDs that were rated using CARS. Mild to moderate autism was recorded in 25.71% of group I compared to none of controls and their CARS' total score was significantly negatively correlated with serum level of 25 hydroxy vitamin D.

Zaky et al., (2015) [10] concluded that ASDs do occur in vitamin D deficient/insufficient rachitic infants and children with a documented significant negative correlation between 25 (OH) vitamin D and the total CARS' score i.e. the lower the 25 (OH) vitamin D, the higher the total CARS' score, the severer the autistic manifestations. Accordingly, future studies are recommended on Egyptian nationwide representative samples of vitamin D deficient/insufficient rachitic infants and children to determine the actual magnitude of the problem in Egypt, the developing country that in spite of being sunny almost all through the year still the Egyptian infants and children are showing vitamin D deficiency/insufficiency as well as autism.

It is well known that environmental as well as genetic factors are important in the etiology of autism [11]. Fernell et al., (2010) [12] have reported that different environmental factors contributing to vitamin-D deficiency are also associated with increased risk of autism. So, association of vitamin D deficiency and ASDs seems not to be a mere hypothesis after it has been supported by the findings of many studies including ours [10]. Vitamin D is crucial for several key physiological processes, including brain development, DNA repair, and regulation of many genes. Much evidence indicates that prenatal and early postnatal vitamin-D deficiency increases autism risk, probably through multiple effects, including impaired brain development and increased de novo mutations [13, 14].

Interestingly, Patrick and Ames (2014) [15] presented an evidence that vitamin D hormone (calcitriol) activates the transcription of the serotonin synthesizing gene tryptophan hydroxylase 2 (TPH2) in the brain at a vitamin D response element (VDRE) and represses the transcription of TPH1 in tissues outside the blood-brain barrier at a distinct VDRE. They claimed that the proposed mechanism explains 4 major characteristics associated with autism: the low concentrations of serotonin in the brain and its elevated concentrations in tissues outside the blood brain barrier; the low concentrations of the vitamin D hormone precursor 25-hydroxyvitamin D [25(OH) D3]; the high male prevalence of autism; and the presence of maternal antibodies against fetal brain tissue. Because of the foregoing accumulated evidence based on reports of many investigators, it is recommended to screen for ASDs in vitamin D deficient/insufficient rachitic infants and children as a high risk group for the development of such disorders and to treat them as prompt as possible with proper doses of vitamin D which could represent a magic therapeutic modality for a disorder with such complex pathogenesis like autism. On the other hand, it is advisable to biologically screen autistic children for vitamin D deficiency/insufficiency and treat them with proper doses of this vitamin whenever deficient or insufficient. Lastly, but by no means least, creating public awareness about the importance of vitamin D for both physical and mental health of infants and children and the necessity of reasonable sun exposure with adequate vitamin D supplementation is crucial [10].

References

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