Medicine

THE RISK OF VITAMIN D DEFICIENCY AND EPILEPSY

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ABSTRACT:
WE HAVE NOTICED LATELY AN INCREASED FOCUS ON VITAMIN D DEFICIENCY IN RECENT YEARS. CHILDREN WITH LOW VITAMIN D LEVELS ARE AT RISK OF ABNORMAL BONE MINERALIZATION AND ARE LINKED TO POOR BONE HEALTH IN EPILEPSY PATIENTS, TREATED WITH ANTICONVULSANT MEDICATION FOR MANY YEARS. HOWEVER, VITAMIN D IS NOT THE ONLY FACTOR DETERMINING OF BONE HEALTH IN CHILDREN WITH EPILEPSY. ANTICONVULSANT MEDICATION, IN ADDITION TO COMORBIDITIES OF EPILEPSY AND COEXISTING NEUROLOGIC DISEASES, ARE IMPORTANT FACTORS IN THIS COMPLEX TOPIC. WE ARE REVIEWING THE TYPES OF POPULATIONS AT RISK AND WE ARE ALSO DISCUSSING THE EXPERT OPINIONS REGARDING VITAMIN D ALGORITHMS FOR SCREENING AND TREATING VITAMIN D INSUFFICIENCY IN THESE PATIENTS.

KEY WORDS: *VITAMIN D, DEFICIENCY, ANTIEPILEPTIC DRUGS, EPILEPSY, CHILD*

Vitamin D is a steroid hormone and in recent studies it is mentioned as a neurosteroid hormone, because it was demonstrated that vitamin D is related with some neurological disorders. Furthermore, vitamin D receptors are spread in the brain structures.

Epilepsy represents a neurological pathology and although described since antiquity, it still remains interesting, highly polymorphic and even challenging when it comes to treatment. Usually this diagnosis triggers antiepileptic treatment, necessary for long periods of time, often exceeding two years. Symptomatic epilepsies (seizures being the consequence of another disease/ lesion) require continuous medication most of the times. In pediatric neurology, epilepsy represents a major pathology section, inducing anti-seizure treatment which have metabolic repercussions, highly dependent on the child's age at the time of the onset of the disease.

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One of the hot topics in medical literature has been, for more then 10 years, the study of vitamin D deficiency in AED treated children. "Old" AEDs include: Carbamazepine, Clonazepam, Ethosuximide, Phenobarbital, Phenytoin and Valproate. "New" AEDs include: Lamotrigine, Levetiracetam, Oxcarbazepine, Topiramate, Vigabatrin, Zonisamide, Felbamate and Gabapentin. Carbamazepine, Phenobarbital and Phenytoin were considered enzyme-inducing antiepileptic drugs (AEDs) and the others were not. Patients treated with more than one AED were classified as taking "old" or "enzyme-inducing" AEDs if at least one of their prescribed medication fell into these categories.

Over time, constantly increasing evidence linked a variety of biochemical, metabolic and radiological abnormalities in the bone to the use of antiepileptic drugs (AEDs). Although women and children are at particular risk, bone loss associated with AED use happens at all ages in both sexes. However, the awareness of the effects of AEDs on bone health among the physicians treating patients with epilepsy is quite low. Usually, vitamin D deficiency associated with AED treatment is largely unrecognized and consequently untreated.

Enzyme-inducing AEDs have been demonstrated to have side effects on bone health, ever since the seventies. Recently, international studies have shown that the use of non-enzyme-inducing AEDs including valproate and newer AEDs may induce vitamin D deficiency[4]. Enzyme-inducing AEDs are known to accelerate the metabolism of vitamin D, resulting in inactive metabolites, decreased fractional calcium absorption, secondary hyperparathyroidism with greater bone resorbtion, and higher rates of bone loss. Studies of valproate and calcium levels are still contradictory and the possible mechanisms for the higher rates of bone loss with the use of non-enzyme-inducing newer AEDs have not yet been elucidated[5].

There are recommendations to test patients before starting and during antiepileptic treatment and interesting results have been recently published [6].

The prevalence of inadequate vitamin D levels in pediatric epilepsy patients is significant, even if the rate is comparable to the general population. These children are at additional risk of bone injury due to their seizures, comorbid neuromotor dysfunction and long-term treatment with medication that affect bone health both through vitamin D metabolism and other mechanisms. Therefore screening and treating low vitamin D levels is worthwhile in pediatric epilepsy patients. The test and also the treatment, in case of deficiency, do not have significant side effects, and may improve bone health in this vulnerable population.

The optimal dose of vitamin D to be given to patients with epilepsy remains unclear. Therefore, the multidisciplinary team who treats an epileptic child must include an endocrinologist, who should monitor the metabolic and radiologic parameters, in each of the patients on an AED treatment.

Vitamin D deficiency has been lately reanalyzed not only in breast fed infants and toddlers , but also in young, middle aged and older adults. Vitamin D deficiency and its consequences are extremely subtle, but have various and very important implications for human health.

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„We consider necessary a program to educate the public and the general practitioners, that not only should they be caring about blood cholesterol levels, but they should also be aware of their vitamin D status, i.e., 25-hydroxyvitamin D levels"[7].

The lower limit of the normal range for 25-hydroxyvitamin D was debated for a long time. In June 6, 2011 The Endocrine Society elaborated a document: "Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline", marking a real breakthrough in vitamin D protocols worldwide[8]. Vitamin D deficiency was defined as a 25-hydroxyvitamin D below 20 ng/mL and vitamin D insufficiency as a 25(OH)D levels between 21 ng/mL to 29 ng/mL. This task force recommended that the level of serum circulating 25(OH)D should be tested for a correct diagnosis. The experts also recommended the screening of vitamin D deficiency only in individuals at risk of deficiency, including obese children and adults (BMI ≥30), black and Hispanic children and adults, pregnant and lactating women, and patients taking certain medication such as glucocorticoids and AIDS therapy.

It is not advisable to use 1,25-dihydroxyvitamin D assay and its use is only recommended in certain conditions, such as acquired and inherited disorders of vitamin D and phosphate metabolism.[9]

Daily dietary intake recommendations based on age, the target being to maximize bone health include: infants and children aged 0 to 1 require at least 400 IU and children aged 1 to 18 require at least 600 IU. To raise 25(OH)D levels above 30 ng/mL may require at least 1,000 IU. The guidelines also stipulated tolerable upper limits of vitamin D which should not be exceeded without medical supervision: 1,000 IU per day for infants up to 6 months, 1.500 IU per day for infants from 6 months to 1 year, at least 2,500 IU per day for children aged 1 to 2 ; 3,000 IU per day for children aged 4 to 8 and 4,000 IU per day for everyone over 8 years of age. They state the fact that higher levels of 2,000 IU per day for children aged 0 to 1 ; 4,000 IU per day for children aged 1 to 18 ; and 10,000 IU per day for children and adults aged 19 and older may be needed to correct vitamin D deficiency," the task force stated [10]

The experts made special considerations regarding treatment with vitamin D_2 or D_3 for vitamin D-deficient patients. A two- to three-times higher dose of vitamin D is recommended for obese patients, patients with malabsorption syndromes and patients taking medications that may affect vitamin D metabolism.(The dose may be 6,000 IU to 10,000 IU per day to maintain a 25(OH)D level above 30 ng/mL, followed by maintenance therapy of 3,000 IU to 6,000 IU. Several studies suggest that higher doses may be preferable to lower doses, both in adults and children.[11]

There are currently no widely accepted guidelines for treating diseases of bone metabolism in epilepsy.

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At present we need to study further larger cohorts of patients, our main focus being on the epileptic child, from our country, with our sunlight conditions, in order to help prevent vitamin D deficiency and the „domino effect" that follows it.

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