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Prevalence of Vitamin B12 Deficiency in West Syndrome: A Retrospective Chart Review

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Abstract

Aims and Objectives:

The aim of this study was to describe the vitamin B12 status among children treated for West syndrome and to review the clinical response to vitamin B12 supplementation among those found deficient.

Materials and Methods:

Hospital records of children with West syndrome with a minimum follow-up of 6 months where serum vitamin B12 was estimated during the course of treatment were identified. Records were studied for etiology, and their response to clinical treatment was noted.

Results:

The two main etiology were cryptogenic in 12 (46.2%), and perinatal asphyxia in 10 (38.5%) children. Serum vitamin B12 levels (levels < 203 pg/mL) were deficient in two (7.7%) children of the 26 eligible records. On vitamin B12 supplementation, both of these children did not achieve any reduction in the frequency of spasm.

Conclusion:

In this limited cross-sectional study, vitamin B12 was deficient in 7.7% of children with West syndrome with lack of reduction in frequency of spasm on B12 supplementation.

KEYWORDS: *Epilepsy*, *infantile spasms*, *micronutrients*, *vitamin B12 deficiency*

INTRODUCTION

West syndrome is an epileptic encephalopathy characterized by epileptic spasm, electroencephalographic (EEG) finding of hypsarrhythmia with or without developmental delay. Predominant cause of West syndrome in India includes perinatal asphyxia (61.4%), neonatal meningitis (10.6%), and postnatal meningitis (11.4%).[1] There is an emerging interest in role of vitamin B12 deficiency in infantile spasm. Majority of our population is strictly vegetarian, resulting in inadequate amount of vitamin B12 in their diet.[2]

Vitamin B12 is essential for synthesis and maintenance of myelin. Vitamin B12 deficiency results in accumulation of methylmalonyl CoA, which gets converted into methylmalonic acid, which is a myelin destabilizer. In addition, disruption of methionine cycle with resultant accumulation of neurotoxic metabolites such as homocysteine is known in vitamin B12 deficiency.[3] Neurological manifestations of vitamin B12 deficiency include hypotonia, developmental delay or regression, apathy, paresthesia, ataxia, dementia, demyelination, infantile tremor syndrome, and rarely seizures.[4]

Seizures and epilepsy are uncommon manifestation of B12 deficiency. There are discrete case reports of children with West syndrome showing spasm cessation and developmental gain with parenteral vitamin B12 treatment.[5,6,7] In a recent study from North India, it was observed that 14 children with West syndrome were B12 deficient as compared to only three children with global developmental delay alone. Among these 14 children, seven, who did not respond to steroids or vigabatrin, failed to show response to vitamin B12 supplementation as well.[8]

This study finding in addition to discrete case reports leads us to possible role of vitamin B12 deficiency in children with West syndrome. With this background, this study was designed to review the hospital records of children with infantile spasm for their vitamin B12 level and their response to vitamin B12 supplementation.

MATERIALS AND METHODS

This study was conducted in Pediatric Neurology Clinic of a tertiary care teaching hospital of North India. It was a retrospective chart review of all patients diagnosed with West syndrome from July 2016 to July 2018. Children were diagnosed with West syndrome, on the basis of the triad of infantile spasms, hypsarrhythmia or its variant on EEG, and developmental regression or delay. Hospital records of children with West syndrome where serum vitamin B12 was estimated during the course of treatment were identified. Children with history of blood transfusion, those on multivitamin supplements and those with a follow-up period of less than 6 months, were excluded from the study.

Data pertaining to demographic and clinical profile, age at onset, age at presentation, age at diagnosis, number of clusters, number of spasm per cluster, and other co morbidities were noted. Perinatal events, developmental milestones, and relevant family history were retrieved. Physical examination findings of tone abnormalities, microcephaly, neurocutaneous markers, dysmorphism, and organomegaly were also noted. EEG and magnetic resonance imaging findings were retrieved. As a part of our institute protocol, children with West syndrome with clear perinatal insult are treated sequentially with steroids, vigabatrin, valproate, clonazepam, levetiracetam, topiramate, and modified Atkins diet in that order. Records were studied for treatment response, time taken to respond, any evidence of relapse, and evolution to other seizure types. Timing of serum vitamin B12 levels in relation of stage and response to treatment was recorded.

Serum vitamin B12 level was measured by chemiluminescent immunoassay, in which vitamin B12 in the sample competes with a fixed amount of vitamin B12 on the solid-phase supporter for sites on the biotinylated detection Ab specific to vitamin B12. Children with serum vitamin B12 levels lower than 203 pg/mL were considered B12 deficient.[9] The data collected were then compiled into Microsoft Excel sheet (Microsoft, 2007 Version, Washington, Unites State). Categorical variables were presented as proportions (%) and continuous variables as mean (standard deviation [SD]) or median (interquartile range [IQR]).

Results

Medical records of 26 children were finally analyzed. The mean (SD) age at onset of spasm was 4.1(3.6) months. The mean age at diagnosis was 11.9(6.2) months. The mean (SD) lag time to treatment was 8.5(7.4) months. There was a male preponderance (*n* = 20 [76.9%]) in our study. Most of them (*n* = 22[84.6%]) were preterm with birth weight less than 2.5 kg. The most common cause of West syndrome in the selected case records was cryptogenic 12(46.2%) followed by birth asphyxia 10(38.5). Average clusters among enrolled patients were 5.3 clusters per day, with each cluster having 6.5 spasms. EEG findings were consistent with classical hypsarrhythmia in 7(26.9%) children [Table 1].

The mean (SD) serum vitamin B12 level was 526.2 (399.0) pg/mL, and the median (IQR) value was 374.5 (279.25–718.25) pg/mL [Table 2]. Only two (7.7%) children with West syndrome were vitamin B12 deficit; both were preterm with birth weight less than 2.5 kg. Mean (SD) age at onset of spasm was 4.5(4.9) months, and average clusters were 3.5(0.7) clusters per day, with each cluster having 4.5(0.7) spasms. One of them had hypoxic ischemic encephalopathy and the other had no definitive etiology (cryptogenic). EEG in both of them revealed modified hypsarrhythmia. There was no spasm reduction despite vitamin B12 therapy. Vitamin B12 (oral) was administered in the dose of 1000mg per day for 7 days followed by weekly for 4 weeks followed by monthly for 6 months.

Discussion

Our cohort revealed that only two of 26 children treated with West syndrome had vitamin B12 deficiency. Both children did not respond to vitamin B12 supplementation. Lack of this clinical response to vitamin B12 supplementation was also observed by previous authors.[8]

Observation of vitamin B12 deficiency among children with West syndrome despite lack of clinical response in a limited number of patients rekindles our mind to possible role of vitamin B12 in treatment of this drug resistant epilepsy.

Vitamin B12 is a water-soluble vitamin, not synthesized in human body; it is mostly found in foods of animal origin. It plays a major role in normal functioning of nervous system, DNA synthesis, regulation of fatty acid metabolism, and formation of blood.[10] Infants are particularly prone to B12 deficiency often secondary to low levels of B12 in the breast milk of otherwise asymptomatic B12-deficient mothers. Classical manifestations include cognitive regression, tremors, developmental delay, hypotonia, and lethargy. Epilepsy as a clinical manifestation of B12 deficiency is uncommon. Literature revealed an interesting report of an infant with vitamin B12 deficiency treated with B12 supplementation who subsequently developed infantile spasm.[11] Considering these discrete reports, it is very difficult to discard the association of B12 deficiency with infantile spasm. There is emerging interest of micronutrient deficiency in children with drug-resistant epilepsy. If not causative, one keeps wondering if this micronutrient deficiency contributes to the burden of seizures in infants with drug resistant epilepsy.

Meena *et al*.[8] conducted a systematic study to show association of vitamin B12 deficiency in children with infantile spasms. They found that children with infantile spasms had lower mean serum vitamin B12 levels and elevated serum homocysteine levels and urinary methylmalonic acid levels as compared to the children with global developmental delay without spasms. In their study, 14 (35%) of 40 cases of infantile spasms had vitamin B12 deficiency as compared to three children with vitamin B12 deficiency in group with global developmental delay.[8] In contrast, our study revealed that only two children were vitamin B12 deficient, and three had subnormal vitamin B12 levels among the 26 enrolled children.

There are anecdotal case reports of spasm cessation with vitamin B12 supplementation in a 6-month and a 10-month-old infant with West syndrome with documented B12 deficiency.[5,7] Similar findings of cessation of spasm and resolution of EEG findings have been reported by authors from Turkey, where two infants with cryptogenic West syndrome treated conventionally with adrenocorticotropic hormone (ACTH) and phenobarbitone along with B12 supplementation. It remains ambiguous whether vitamin B12 worked or did ACTH work in these infants. This thought generates from comparison of one of similar child with cryptogenic West syndrome in our cohort who did not respond to vitamin B12 supplementation. Although there was no clinical response even in the other child with perinatal asphyxia, it is difficult to generalize findings of nonresponse to B12 therapy considering that only two kids had B12 deficiency.

This study explores the avenue of potentially treatable vitamin B12 deficiency among infants with West syndrome. However, the retrospective nature of data collection with review of records of only selected group of children where vitamin B12 levels were performed with at least 6-month follow-up were major limitations of the study. Limited sample of 26 children with lack of age-matched control and possibility of falsely low vitamin B12 levels as serum homocysteine levels were not estimated were some of the other limitations. Hence, the findings of vitamin B12 deficiency and lack of clinical response to vitamin B12 therapy observed in this study needs to be interpreted in the context of these limitations.

To conclude, serum vitamin B12 deficiency was seen in only in two of 26 enrolled children with West syndrome, who did not achieve any reduction in frequency of spasm with B12 supplementation. However, considering cross-sectional type of study design, lack of age-matched con-

trols, and limited sample size, further randomized control trials are suggested to compare the efficacy of additional B12 supplementation among children with West syndrome receiving conventional therapy.

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Conflicts of interest

There are no conflicts of interest.

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Figures and Tables

Table 1:

Baseline clinical profile of children with West syndrome (*n* = 26)

Baseline characteristics	Values
Mean (SD)	
Age (months)	13.2(7.5)
Age at spasm onset (months)	4.1(3.6)
Age at diagnosis (months)	11.9(6.2)
Number of clusters per day	5.3(1.9)
Number of spasms per cluster	6.5(3.4)
Number (%)	
Males	20(76.9%)
Preterms	22(84.6%)
Birth weight (<2.5 kg)	22(84.6%)
Development prior to spasm onset	
Developmental delay present	19(73.1%)
Development normal	07(26.9%)
Cerebral palsy	10(38.5%)
Microcephaly	10(38.4%)
Etiology based on neuroimaging	
Unknown cause (cryptogenic)	12(46.2%)
Birth asphyxia	10(38.5%)
Perinatal stroke	1(3.8%)
Kernicterus	1(3.8%)
Metabolic cause	1(3.8%)
Inborn error of metabolism	1(3.8%)
Number (%)	
EEG finding	
Classical hypsarrythmia	7(26.9%)
Modified hypsarrythmia	13(50%)
Multifocal epilepsy	4(15.4%)
Not known	2(11.5%)

SD = standard deviation

Table 2:

Serum vitamin B12 levels in the study participant (*n* = 26)

Serum vitamin B12 levels, pg/mL	
Mean (SD)	526.1 (399.0)
Median (IQR)	374.5 (279.25, 718.25)
Children with vitamin B12 deficiency*, *n* (%)	2 (7.7)
Children with normal vitamin B12 levels, *n* (%)	21 (80.8)

IQR = interquartile range (25th and 75th percentiles), SD = standard deviation

*Serum vitamin B12 level <203 pg/mL was considered B12 deficiency