

Infants with vitamin B12 deficiency-related neurological dysfunction and the effect of maternal nutrition

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Abstract

Aim: Studies linked vitamin B12 deficiency in infancy are most commonly in patients with hematological and dermatological complaints rather than infant with neurodevelopmental retardation. In our study we aimed to evaluate the data of infants who presented with various neurological complaints and determined neurodevelopmental retardation due to vitamin B12 deficiency and also effects of maternal diet on the infants.

Material and Methods: Infants who were admitted with various neurological complaints due to vitamin B12 deficiency between the dates of September 2016 and March 2018 were included in this study. Patients were retrospectively analyzed according to age, growth and development, clinical and laboratory findings (neurological, hematologic), continuation of breastfeeding, age at onset of complementary food. During the pregnancy and lactation, the amount of feeding with animal foods, intake of vitamin supplements, duration of breastfeeding and vitamin B12 levels were examined.

Results: The most common complaints were fatigue, pallor, no eye contact, apathy, vomiting, constipation, diarrhea, refusal to feed, retardation to growth and development, undeveloped or lost of ability (ability to tonic neck reflex, ability to sit supported and unsupported ability to sit). In the neurological examination of infants; in 13 infants, there was hypotonia, undeveloped ability to tonic neck reflex and ability to sit (supported and unsupported). Fifteen, in 15 infants just undeveloped ability to sit (supported and unsupported) and also in 6 infants had swallowing disorders.

Conclusion: Vitamin B12 routinely to all pregnant women like folic acid and iron supplementation. In addition, developmental stages of infants should be evaluated and vitamin supplements should be given to infants when necessary.

Keywords: Breastfeeding; Infant; Neurological Findings.

INTRODUCTION

The deficiency of vitamin B12, which has an important role in ensuring healthy growth and development in children, is a health problem in all age groups, especially in developing countries (1-3). Deficiency of B12 vitamins if not diagnosed and treated early in infant period where the growth and development is very rapid which are very important for the construction of DNA, RNA and neurotransmitters, can lead to irreversible neuromotor pathologies (3,5).

Vitamin B12 is one of the most complex vitamin molecules. Deficiency of this vitamin is one of the important causes of retardation of growth and development in the infancy period because of essential molecule for lipid metabolism, carbohydrate metabolism, energy production, protein synthesis. Because it cannot be synthesized in the human body and nutritional sources are only animal products,

people who are unable to access these foods and strict vegetarians should receive vitamin B12 support (3). The most common cause of deficiency of vitamins in infants is inadequacy in the maternal diet. These infants are the babies whose mothers, have low socioeconomic status or fed with strict vegetarian diet (4). Although brain development continue from the first days of intrauterine life until adolescence, a significant part of this period is occur in the fetal and infant period. In addition myelination which determines the communication between neurons, takes place in same period. So nutritional deficiencies adversely affect both brain development and myelination (1,3,4,6-8). Babies of pregnant women with normal serum levels of vitamin B12, start living with vitamin reserves sufficient for their healthy development for between 6 months and 1 year. Unfortunately, because of the babies of pregnant women with vitamin deficit are born

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with inadequate vitamin reserves. Despite these babies healthy at birth, neurological symptoms due to deficiency of vitamin occur frequently first 4-6 months (2,4,8). World Health Organization; recommends that pregnant women, breastfeeding mothers, as well as infants receive vitamin B12 support (1). However, it is stated in the literature that daily intake is estimated to be well below the recommended level (5,8). Clinical findings related to vitamin B12 deficiency may be different in childhood age groups (4,9). Many different clinical manifestations can be observed, ranging from asymptomatic clinical findings to growth and development retardation, hematological, gastrointestinal, mucocutaneous and neurological problems (2,4,5,10). Delay of the diagnosis in infancy may cause permanent neurological findings. Therefore, early diagnosis and treatment is important (3, 7,9,11). Studies linked vitamin B12 deficiency in infancy are most commonly in patients with hematological and dermatological complaints rather than infant with neurodevelopmental retardation. Early recognition and treatment of vitamin B12 deficiency in infants may prevent the development of irreversible neurological deficits. We aimed to evaluate the data of infants who presented with various neurological complaints and determined neurodevelopmental retardation due to vitamin B12 deficiency and also effects of maternal diet on the infants.

MATERIAL and METHODS

Our study was started after acceptance of Hatay Mustafa Kemal University Medicine Faculty ethics committee (2018 / 18153). Infants who were admitted with various neurological complaints due to vitamin B12 deficiency between the dates of September 2016 and March 2018 were included in this study. All patient files were scanned retrospectively. Verbal consent was obtained from the patients.

Patients were retrospectively analyzed according to age, growth and development, clinical and laboratory findings (neurological, hematologic), continuation of breastfeeding, age at onset of complementary food.

During the pregnancy and lactation, the amount of feeding with animal foods, intake of vitamin supplements, duration of breastfeeding and vitamin B12 levels were examined.

Vitamin B12 deficiency was diagnosed according to clinical findings, hematological evaluations, low serum B12 levels and normal serum folate levels of infants and nutritional history (infants and mothers).

Vitamin B12 level was measured by direct chemiluminescence competitive system (Siemens advia centaur XP).

Vitamin B12 deficiency was accepted in patients with B12 levels below 200 pg/dL and normal serum folate levels.

Leukocyte level below 4500/mm³ were defined as leukopenia, platelet level below 150.000/ mm³ were defined as thrombocytopenia (12).

Hematological findings of vitamin B12 deficiency were evaluated with hemogram and peripheral blood smear.

The diagnosis of megaloblastic anemia was based on increased mean erythrocyte volume (MCV), hypersegmentation in neutrophils, low B12 level and normal folate level.

Infants with a history of small gestational age, prematurity, asphyxia in the perinatal period, chronic disease, metabolic disease and history of central nervous system infection were excluded from the study.

Vitamin B12 (Dodexampul, Deva, 1 mg cyanocobalamin) was given to infants and their mothers.

Patients after 3 months of treatment were evaluated.

All categorical data are expressed as number (n) and percentage (%).

RESULTS

The median age of 34 infants was 8 (3-18) months in this study. 19 Nineteen patients (55.88%) was were males and 15 patients (44.12%) was were females.

Of the infants, 11 were exclusively breastfed and 23 were fed with breast milk + infant formula.

The most common complaints were fatigue, pallor, no eye contact, apathy, vomiting, constipation, diarrhea, refusal to feed, retardation to growth and development, undeveloped or lost of ability (ability to tonic neck reflex, ability to sit supported and unsupported ability to sit).

The percentile values (height, weight, head circumference) of the infants were determined. 7 Seven infants were in 3-10 percentile, 8 infants were in 10-25 percentile, 9 infants were under 3 percentile.

In the neurological examination of infants; in 13 infants, there was hypotonia, undeveloped ability to tonic neck reflex and also ability to sit (supported and unsupported), in 15 infants just undeveloped ability to sit was seen in 15 infants (supported and unsupported) and in 6 infants swallowing disorder was observed in 6 infants (Table 1).

In addition, 22 patients had iron deficiency anemia, 6 patients had bisitopenia (leukopenia + anemia), and 2 had pancytopenia (leukopenia + anemia + thrombocytopenia). The mean erythrocyte volume of 15 patients with iron deficiency was normal (coexistence of iron and vitamin B12 deficiency).

Hypersegmentation was observed in neutrophils in the peripheral smears of all infants.

The serum levels of vitamin B12 in infants were determined under 200 pg / dl in 18 infants, under 150 pg / dl in 9 infants, under 95 pg / dl in 7 infants. The serum levels of vitamin B12 of all mothers was under 250 pg / dl.

Breastfeeding were continued in all infants. The median age of onset to complementary food in infants was 5.2 (4.7-6.4) months. Complementary foods were boiled rice, pasta, bread, yogurt, cow's milk, and infant formula.

Table 1. Complaints and clinical findings of infants

	n	%
Complaints		
Weakness	34	100
Pallor	27	79.4
No eyecontact	4	11.7
Apathy	17	50
Vomiting	19	55.8
Constipation	9	26.4
Diarrhea	11	32.3
Refusefeeding	13	38.2
Growthretardation	26	76.4
Undevelopedof ability*	28	82.3
Lost ofability*	6	17.6
Growthand Development Assessment		
>3 percentile	9	25.4
3-10 percentile	17	50
10-25 percentile	8	23.5
NeurologicalFindings		
Hypotonia	13	38.2
Undeveloped ability to tonic neck reflex	13	38.2
Undeveloped ability to sit	28	82.2
Swallowing disorder.	6	17.6
*Abilities of tonicneckreflexandabilityto sit supportorunsupport		

The frequency of feeding with animal products of all mothers during pregnancy and lactation was low. Although they were not regular receive iron and folate supplements during pregnancy, they did not never receiving vitamin B12 supplement during pregnancy and lactation.

Infants reached normal neurodevelopmental levels and percentile values after 3 months of vitamin B12 treatment.

DISCUSSION

The most common cause of vitamin B12 deficiency in infants is nutritional and may be associated with neurological findings. In our study we aimed to sign that early recognition and treatment of vitamin B12 deficiency in infants who vitamin B12 deficiency be occurred due to effects of maternal diet on the infants may prevent the development irreversible neurological deficits.

Symptoms of vitamin B12 deficiency occur between the 4th and 18th months of life. It is reported in the literature that delay in the diagnosis and treatment of infants may cause permanent neurological damage (3,4,8). The most common complaints due to deficiency of vitamin B12 are pallor, jaundice, weakness, vomiting, diarrhea, glossitis, malnutrition, growth retardation, hyperpigmentation of palms and joint surfaces in the literature (4). In accordance with the literature the median age of 34 infants with vitamin B12 deficiency was 8 (3-18) months in our study.

The most common complaints other than neuromotor findings were weakness, pallor, malnutrition, growth and growth retardation. Other complaints were apathy, vomiting, constipation, and diarrhea.

In our study the percentile values (height, weight, head circumference) of the infants were determined. 7 infants were in 3 -10 percentile, 8 infants were in 10-25 percentile, 9 infants were under 3 percentile. Findings related to vitamin B12 deficiency differ according to age in children. Although the clinical manifestations in infant period often occur between 4-18 months, the fact that symptoms are not specific. Therefore may be difficult early diagnosis and treatment (3,4,11). Neurological manifestations due to deficiency of vitamin B12 are frequently reported as irritability, apathy, hypotonia, mental-motor retardation, reduction of deep tendon reflexes, encephalopathy, paresthesia, sensorineural deficits, epileptic seizures, delay or retardation of development, neuropsychiatric changes, involuntary movements in infants. In addition, maternal deficiency is considered to be an independent risk factor for the development of fetal neural tube defect (2-4,11). In the neurological examination of infants; In 13 infants, there was hypotonia, undeveloped ability to tonic neck reflex and ability to sit (supported and unsupported), in 15 infants had just undeveloped ability to sit (supported and unsupported) and in 6 infants had swallowing disorder in this study. Hematological findings related to deficiency of vitamins include anemia, thrombocytopenia, leukopenia, increased MCV and also large-oval erythrocytes and hypersegmentation in neutrophils (> 5 lobe) in peripheral smear (3).

In our study, 22 infants had iron deficiency anemia. The mean erythrocyte volume of 15 infants with iron deficiency was normal. This condition was evaluated as a coexistence of iron and vitB12 deficiency. Six of the infants had bicytopenia (leukopenia + anemia) and two of the infants had pancytopenia (leukopenia + anemia + thrombosiopenia). Hypersegmentation was observed in neutrophils in the peripheral smears of all infants. The importance of vitamin B12 levels for a healthy pregnancy is indicated in the literature. Although vitamin B12 deficiency may be caused by different clinical conditions that cause malabsorption, the most common cause is nutritional causes such as low vitamin B12-containing food intake and strict vegetarianism (2-4,9). Deficiency of vitamin B12 in pregnant and lactating mothers is the main cause of Vitamin B12 deficiency in infants (3,4,8).

At the babies of women with vitamin B12 deficiency due to cannot receive sufficient amounts of vitamin B12 both in prenatal period with placenta and in postnatal period with breastfeeding the severe deficiency of vitamin can be observed (4,5,7). In accordance with the literature the serum levels of vitamin B12 of all mothers was low (> 250pg / dl) in our study. The serum levels of vitamin B12 in infants were under 200 pg / dl in 18 infants, under 150 pg/ dl in 9 infants, under 95 pg / dl in 7 infants.

The World Health Organization and the American

Academy of Pediatrics recommended that infants must receive just breast milk in the first 6 months of life and complementary foods should be initiated after this period and also breastfeeding should continued for up to two years (1,7,8). In our study it was determined that breastfeeding were continued to in all infants. The median age of starting complementary food in infants was 5.2 (4.7-6.4) months. And also it was determined that the preferred as complementary food were boiled rice, pasta, bread, yogurt, cow's milk, infant formula.

Plants are not a good source of vitamin B12. Dietary sources of vitamin B12 are come almost entirely from animal food products. If maternal serum vitamin B12 is sufficient, breast milk is an adequate source of vitamin B12 for infants. However, because of serum low levels of vitamin B12, infants who are breastfeeding by vegetarian mothers are at greatest risk for vitamin B12 deficiency (3,4). In order to prevent deficiency of vitamin B12 in infants, pregnant women and lactating women should be fed with sufficient amounts of animal foods or vitamin supplements (3,4). Because the amount of vitamin B12 in breast milk is related to the amount of vitamin B12 that it takes on diet rather than the mother's stores (2,3,8). In our study, it was learned that none of the mothers were vegetarian but the frequency of feeding with animal product foods during pregnancy and lactation was less than once a month. In addition, it was learned that all mothers were receiving iron and folate supplements although it's not regular however they did not receive vitamin B12 supplement during pregnancy and lactation. Whether or not neurological complications depending on the vitamin B12 deficiency leads to long term sequelae, depends on the severity and duration of vitamin B12 deficiency (2,4,10). Although there is a limited number of data on the long-term prognosis of neurological findings due to deficiency of vitamin B12 in infants, the severity of symptoms and the duration of vitamin deficiency is considered to be the determining factor in the process (5,9,13). Late diagnosis in infants may cause neurological problems, cognitive impairment and severe mental retardation. In the literature, it was shown that normal neuromotor development was achieved in infants who received early diagnosis and treatment before 10 months, while infants who received diagnosis and treatment over 1 year of age may have permanent neurodevelopmental disorders (4,14-17). Therefore, early diagnosis and treatment of vitamin B12 deficiency in infants is very important. In our study, the median age at which the infants were diagnosed was 8 (3-18) months. It was determined that reached normal neurodevelopmental levels and percentile values after 3 months of vitamin B12 treatment with early diagnosis and treatment of these infants.

Vitamin B12 deficiency is one of the causes of neurological findings, anemia, growth and developmental retardation in infants that can be treated. It should be kept in mind that neurological problems due to B12 deficiency may occur even without hematological findings (3,5,9,16,18). Nutritional factors play an important role in the biological

factors affecting the development of the brain in the early period (3,7,12,19).

CONCLUSION

Consequently, early diagnosis and treatment of vitamin B12 deficiency in infants may prevent the development of irreversible neurological deficits, for this reason, we think that should be given vitamin B12 routinely to all pregnant women like folic acid and iron supplementation and developmental stages of infants should be evaluated and vitamin supplements should be given to infants when necessary.

Limitation of the study

In our study, we followed our patients for 3 months. For this reason, prospective studies with longer follow-up are needed in order to evaluate the whether or not neurological complication depending on the vitamin B12 deficiency leads to the long term sequelae the disease.

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