

Anemia, vitamin B12, folic acid and iron deficiency in children who can not feed themselves due to neurological disease

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Summary

Aim: To evaluate malnutrition, anemia and related deficiency of vitamin B12, iron and folic acid in children with neurological disease and related nutritional problems.

Material and Method: In this study, our aim was to investigate anemia and possible reasons such as iron deficiency, folic acid deficiency and vitamin B12 deficiency among patients with nutritional problems who were admitted to Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Outpatient and Service of Pediatric Neurology between June 2010 and December 2010. The study involved a total of 50 patients (30 male and 20 female). A control group including 30 boys and 20 girls was included in the study as well. Complete blood count, iron, folic acid and vitamin B12 values were studied.

Results: A total of 39 patients (78%) had malnutrition; among malnutrition patients 16 (32%) had severe malnutrition, 18 (36%) had moderate malnutrition and five (10%) had mild malnutrition. A total of 22 patients (44%) had anemia, iron deficiency, folic acid deficiency or vitamin B12 deficiency alone or in combination. Nine of 22 patients (18%) had iron deficiency anemia, four (8%) had iron deficiency, five (10%) had folic acid deficiency, one (2%) had folic acid deficiency macrocytic anemia, six (12%) had anemia of chronic disease, two (4%) had B12 deficiency, four (8%) had both iron deficiency anemia and folic acid deficiency.

Conclusions: In our patients with neurological disease, nutritional deficiencies and anemia were found to be quite frequent. These patients should get a special care for nutrition and should be checked periodically for anemia and nutritional parameters. (*Türk Arch Ped 2012; 47: 197-201*)

Key words: Anemia, children, folic acid deficiency, iron deficiency, malnutrition, neurological disease, nutritional deficiency, vitamin B12 deficiency

Introduction

Nutrition is a severe problem in many neurologic diseases in children. The reason for this may be functional disorders related to motor adaptation of the mouth, swallowing and the esophagus, movement problems in sucking, chewing and in the tongue, swallowing dysfunction, laryngeal penetration which leads to aspiration and gastroesophageal reflux. Nutritional problems take an important place in care and treatment of these children. Complications which may develop as a result of malnutrition effect the quality of life in a considerably negative way (1,2). In children with cerebral palsy, the frequency of nutritional problems has been reported to be 30-90% and the rate of malnutrition has been reported to be 90% (1). If nutritional problems are not treated, they can cause morbidity and mortality by leading to malnutrition and to growth and developmental

delay at the end (3,4). In patients with nutritional problems due to neurologic diseases, anemia is observed frequently because of vitamin and mineral deficiencies (5).

In this study, anemia and related iron, folic acid and B12 deficiencies were evaluated in patients with neurologic disease and related nutritional problems.

Material and Method

Patients with nutritional problems and neurologic disease (cerebral palsy, neurometabolic disease, neurodegenerative disease, mitochondrial disease, kernicterus sequela, spinal muscular dystrophy, periventricular leucomalacia, cleft palata and cleft lip) who presented to Kahramanmaraş Sütçü İmam University, Medical Faculty, Outpatient and Ward of Pediatric Neurology between June 2010 and December 2010 were

evaluated prospectively. A total of 50 patients with neurologic disease who could not feed themselves were included in the study. 33 of these patients came from the Pediatric Neurology Outpatient Clinic and 17 came from the Pediatric Neurology Ward. 30 (60%) of the patients were male and 20 (40%) were female. The ages of the patients ranged between 3 months and 16 years (mean 6.35 ± 3.96 years).

Age, gender, height, body weight, diagnosis, the time of the neurologic disease, presence and grade of mental retardation, drugs used, presence of swallowing reflex, feeding route, nutritional product, meal time, meal amount and people who help with feeding were learned and recorded. Hemoglobin, hematocrite, mean erythrocyte volume (MEV), erythrocyte number, platelets, mean erythrocyte hemoglobin concentration (MEHC), leucocyte number, serum iron (SI), serum iron binding capacity (SIBC), ferritin, vitamin B12 and folic acid values were measured.

As the control group 50 patients who presented to the pediatric outpatient clinic, who received diagnoses including acute infection, headache, syncope and febril convulsion, who did not have any chronic disease and who were not being followed up with a diagnosis of anemia were selected randomly with a similar age and gender distribution as the study group.

In the biochemistry laboratory of our hospital, hemogram was tested using "Beckman Coulter LH 750 Analyzer", iron and iron binding capacity were measured using "Siemens Dade Behring Dimension RXLMAX" and ferritin, vitamin B12 and folic acid values were measured using "Siemens Immulite 2000".

Body weight was used to evaluate nutritional status and malnutrition assessment was done according to Gomez classification (6).

In children older than 6 years of age, IQ measurements were done using Wechsler Intelligence Scale (WISC-R) (7).

In patients between 0 and 6 years of age, Ankara Development Screening Inventory (ADSI) which was composed of 154 items answered by the caretaker as "yes" or "no" and in which developmental tests were adjusted according to different age groups was used (8).

The percentile values (p) of the patients between 6 and 18 years of age were found using "growth values of the Turkish children aged 6-18 years" chart which was updated in 2006 (9).

The percentile values of the patients between 0 and 5 years of age were found using "percentiles in the Turkish children aged 0-5 years" chart which was updated in 2007 (10).

A diagnosis of anemia was made using the hemoglobin values recommended by the World Health Organization (WHO) as the lower limits at sea level (<11 g/dL for 6 months-6 years, <12 g/dL for 6-14 years, <13 g/dL for boys older than 14 years, <12 g/dL for girls older than 14 years) (11).

A diagnosis of iron deficiency anemia (IDA) was made, when ID was low, SIBC was high, serum transferrin saturation was below 15%, ferritin was <23 ng/mL, MCV was below 70 or below the normal value for age, RDW was $>15\%$ and hemoglobin level was below the normal value for age (12).

To differentiate thalassemia carrier state hemoglobin electrophoresis was performed in patients who had anemia, hypochromia (low MEHb), microcytosis (low MCV), normal RDW and increased number of erythrocytes.

In our laboratory, normal values for iron, iron binding capacity and ferritin were as follows: iron: 35-150 mg/dL, SIBC: 250-450 mg/dL and ferritin: >23 ng/mL.

The lower limit was accepted to be <193 pg/mL (normal: 193-982) for B12 deficiency and <3 ng/mL (normal: 3-17) for folic acid deficiency (13).

To evaluate the data obtained in the study arithmetic mean (AM) and standard deviation (SD), the minimum value, the maximum value and percentages for age and weight values and distribution percentages in the group for laboratory results were given. In statistical evaluation of the data, p value was calculated using Fisher chi-square test and chi-square test. A p value of $<0,05$ was considered statistically significant. Approval was given by the ethics committee for the study (05.05.2010/200-11/3).

Results

The body weight was between 3,3 kg and 25 kg (mean 14.5 ± 6.33) in female patients and between 5 kg and 49 kg (mean 18.5 ± 10.27) in male patients. 30 (60%) of these patients had a body weight of $<3p$. Height could not be measured, since the patients had contractures due to neurologic disease.

The distribution of diagnoses of the patients is shown in Table 1.

In the control group, 30 of 50 patients were male (60%) and 20 (40%) were female. The ages of the controls were between 45 days and 15 years (mean 6.74 ± 4.08).

In the control group, the body weight was between 9.4 kg and 64 kg (mean 24.92 ± 13.45) in girls and between 5.8 kg and 87 kg (mean 25.37 ± 18.72) in boys. Chi-square test showed that there was no significant difference between the patient and control groups in terms of age ($p > 0.05$).

When the patients were classified according to intellectual state, 34 (68%) had severe mental retardation, 8 (16%) patients had moderate mental retardation and 4 patients (8%) had mild mental retardation (a total of 92%). 4 patients had normal intelligence level.

37 of the patients (74%) were being fed orally, 11 (22%) were being fed by nasogastric route and 2 (4%) were being fed by gastrostomy. When the content of nutrition was evaluated, it was found that 17 (34%) patients were fed with only liquid food products, 19 (38%) were fed with all kinds of foods, 1 (2%) was fed predominantly with cow milk and 13 (26%) were fed with enteral feeding solutions containing 200 calories in 200 ml and prepacked feeding solutions containing 300 calories in 200 ml.

According to Gomez classification 16 patients (32%) had severe malnutrition, 16 (32%) had moderate malnutrition and 7 (14%) had mild malnutrition (a total of 78%). 7 patients (14%) had normal body weight, 2 (4%) were overweight and 2 (4%) were obese.

In the control group, one subject (2%) had severe malnutrition, 8 (16%) had moderate malnutrition and 7(14%) had mild malnutrition (a total of 32%) according to Gomez classification. 24 subjects (48%) had normal body weight, 4 (8%) were overweight and 6 (12%) were obese. When the patient and control groups were compared in terms of malnutrition using chi-square test, a statistically significant difference was found ($p < 0.05$). 12 (32.4%) of 37 patients who were not using enteral feeding solution had severe malnutrition, 14 (37.8%) had moderate malnutrition and 4 (10.8%) had mild malnutrition (a total of 81%).

4 (30.7%) of 13 patients who were using enteral feeding solution had severe malnutrition, 2 (15.3%) had

moderate malnutrition and 2 (15.3%) had mild malnutrition (a total of 61.3%).

24 of the patients (48%) were using antiepileptic drug.

In the patient group, the laboratory values measured for anemia were as follows: Hb: 4.8-15.6 g/dL, serum iron: 10-121 mg/dL, SIBC: 155-577 mg/dL, ferritin: 1-727 ng/mL, B12: 153-10 000 pg/mL, folic acid: 1.6-32.9 ng/mL. 28 patients (56%) were considered to be normal and 22 (44%) patients were considered to be abnormal. 4 (8%) of these abnormal results were only iron deficiency (ID), 9 (18%) were iron deficiency anemia (IDA), 5 (10%) were folic acid deficiency, one (2%) was macrocytic anemia due to folic acid deficiency, 4 (8%) were IDA plus folic acid deficiency. 6 (12%) were evaluated as anemia of chronic disease and 2 (4%) were evaluated as B12 deficiency. No B12 deficiency anemia was found. The results of evaluation of the patients are shown in Table 2.

In the control group, the laboratory values measured for anemia were as follows: Hb: 7.9-15.2 g/dL, serum iron: 1-122 mg/dL, SIBC: 247-415 mg/dL, ferritin: 2.27-516 ng/mL, B12: <150-1273 pg/mL, folic acid: 5.23-30.4 ng/mL. 47 patients (94%) were evaluated to be normal and 3 (6%) were evaluated as iron deficiency anemia.

When the rates of ID in the patient and control groups were compared using Fisher's exact chi-square test, no statistically significant difference was observed ($p > 0.05$). However, 4 (8%) patients in the patient group had ID, whereas there was no ID in the control group. No statistically significant difference was found between the two groups in terms of IDA rates ($p > 0.05$). While 2 patients (4%) had B12 deficiency, 5 patients (10%) had folic acid deficiency and one patient (2%) had folic acid deficiency anemia in the patient group, none was found in the control group. When compared using Fisher's exact chi-square test, no statistically significant difference was observed ($p > 0.05$). An association of iron deficiency anemia and folic acid deficiency was found in 4 (8%) patients in the patient group, while it was not found in the control group. When compared using Fisher's exact chi-square test, no statistically significant difference was observed between

Table 1. Distribution of neurologic diseases by diagnoses

| Primary disease | Number (n) | Percentage (%) |
|------------------------------------|------------|----------------|
| Cerebral palsy | 12 | 24 |
| Periventricular leukomalacia | 10 | 20 |
| Hypoxic ischemic encephalopathy | 10 | 20 |
| Brain developmental anomaly | 2 | 4 |
| Autism | 2 | 4 |
| GM1 Gangliosidosis | 2 | 4 |
| Intrauterine CMV infection sequela | 1 | 2 |
| Cernicterus | 5 | 10 |
| Spinal muscular atrophy | 2 | 4 |
| Rett Syndrome | 1 | 2 |
| Meningitis sequela | 1 | 2 |
| Degenerative brain disease | 1 | 2 |
| Metabolic disease | 1 | 2 |
| Neuronal Ceroid Lipofuscinosis | 2 | 4 |
| West syndrome | 1 | 2 |
| Syndromic patient | 1 | 2 |

Table 2. Comparison of the laboratory results of the patient and control groups

| | Patient group number (percentage) | Control group number (percentage) | p |
|--|-----------------------------------|-----------------------------------|---------|
| Iron deficiency | 4 (8%) | 0 | 0.117 |
| Iron deficiency anemia | 9 (18%) | 3 (6%) | 0.064 |
| Folic acid deficiency | 5 (10%) | 0 | 0.056 |
| Folic acid deficiency anemia | 1 (2%) | 0 | 1 |
| B12 deficiency | 2 (4%) | 0 | 0.494 |
| B12 deficiency anemia | 0 | 0 | 1 |
| Anemia of chronic disease | 6 (12%) | 0 | 0.026 * |
| Iron deficiency anemia + folic acid deficiency | 4 (8%) | 0 | 0.117 |
| Normal | 28 (56%) | 47 (94%) | 0.00 * |

* : Statistically significant ($p < 0.05$)

the two groups ($p>0.05$). Anemia of chronic disease was found only in 2 patients in the patient group. This difference was found to be statistically significant using Fisher's exact chi-square test ($p<0.05$). When the variables in our study were evaluated generally, percentage rates of the subjects with abnormal values were significantly higher in the patient group ($p<0.05$).

Discussion

In the literature, we could find no study examining anemia and iron, folic acid and B12 deficiencies in association in patients with malnutrition due to neurologic disease. Limited number of studies have been performed on these subjects. There is one study in which IDA was examined in patients with cerebral palsy and one study in which iron deficiency, IDA and B12 deficiency were examined in patients with cerebral palsy (5,14). Our study is the first study evaluating malnutrition developed as a result of nutritional deficiency due to neurologic disease and iron, folic acid and vitamin B12 states, though the number of patients included was low.

In children with neurologic disease, nutrition is a very important problem. Since 48 (96%) of our patients had severe mental retardation, nutrition in these patients was dependent on the mother. This really shows that nutrition was a severe problem in our patients. The frequency of nutritional problems in children with cerebral palsy has been reported to be 30-90% (1). In our study group, the rate of malnutrition according to Gomez classification was found to be 78%. This rate was 81% in patients who were using prepacked feeding solutions and 61.3% in patients using enteral feeding solutions. The fact that the rate of malnutrition was lower in patients who were using enteral feeding solutions compared to the ones who were not using enteral feeding solutions suggests that enteral feeding solutions may be beneficial in prevention of malnutrition because of convenience of intake (15).

In the study performed by Kabakuş et al. (16), malnutrition was found in an important proportion (40%) of the patients and 75% of these patients had moderate and severe malnutrition and 25% had mild malnutrition. In a study performed in Spain, serum biochemical values (albumin, transferrin, ferritin, iron, calcium, phosphorous, cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride, alkaline phosphatase, transaminase and carnitine) were examined in 128 children with mental retardation and malnutrition was found in the majority of children (74%) with mental retardation (17). In our study, we found a higher rate of malnutrition in our patients (78%) compared to the study performed by Kabakuş et al. (16). This may be due to the fact that our study group was composed of patients who had neurologic disease.

37 (74%) of our patients were being fed orally, 11 (22%) were being fed by nasogastric route and only 2 (4%) were being fed by gastrostomy. One of the two patients with gastrostomy had severe malnutrition and feeding with gastrostomy was started one month before the study in this patient. The other patient who

was being fed by gastrostomy had a normal body weight. The low rate of feeding by gastrostomy (4%) suggests that use of gastrostomy has not become widespread among patients with malnutrition due to neurologic disease. Families are not open to gastrostomy because of various reasons (unpleasant appearance, fear of intervention, concern that the status of the patient would deteriorate etc.). In children with malnutrition, motor efficiency has been observed to be increased by supporting nutrition using appropriate diets and the rates of anemia have also decreased (18). Special interest should be given to feeding of patients who have problematic and inadequate nutrition and family support should be sought for opening gastrostomy at an early stage, if required.

In children with neurologic disease, problems related to swallowing, reflux and anemia, ID, folic acid deficiency and B12 deficiency because of rigidity and dependency to a second person for feeding are observed frequently (5). Findings of anemia, ID, folic acid and B12 deficiency were found in 22 of our patients (44%). 4 of these (8%) had ID and 9 (18%) had IDA. In a study performed by Ayata et al. (14) in 40 patients with cerebral palsy, IDA was found in 40% of the patients. In the study performed by Papadopoulos et al. (5) in Thessaloniki, Greece in 108 patients with cerebral palsy, ID was found with a rate of 38% and IDA was found with a rate of 33%. In the study performed by Hong et al. (19), anemia was found in 50.2% of 229 patients with cerebral palsy and 22.2% of these patients had IDA. The reason that we found a lower rate of anemia in our patient group compared to the above mentioned studies may be improved medical care services, since it is a more recent study.

In our patient group, 6 patients (12%) had anemia of chronic disease. Anemia of chronic disease is an expected finding in these patients (20).

5 of our patients (10%) had folic acid deficiency, one (2%) had anemia related to folic acid deficiency and 2 (4%) had B12 deficiency. No B12 deficiency anemia was found. Folic acid deficiency or B12 deficiency was not found in the studies of Papadopoulos et al. (5) and Ayata et al. (14). However, Lee et al. (21) reported folic acid deficiency due to malnutrition and related megaloblastic anemia in a patient with cerebral palsy. Our study suggests folic acid deficiency or B12 deficiency can also be observed in patients with malnutrition due to neurologic disease, though with a small proportion.

Conclusively, malnutrition and iron deficiency are important problems in patients with neurologic disease, though there are few studies performed on this subject. Nutritional problems in these patients should be cared about, families should be informed about resolving of malnutrition and it should be explained that gastrostomy would be more appropriate, if oral treatment is inadequate. Correction of anemia with appropriate nutrition can help to increase motor efficiency and to improve the quality of life.

Conflict of interest: None declared.

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