Effects of Multivitamin and Folic Acid Supplementaion in Malnourished Children

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Abstract

Objective : To study the effect of multivitamin and folic acid supplementation on serum folate level and weight gain.

Material and Method : A prospective randomized controlled study was conducted in malnourished children at the Nutrition Clinic, Queen Sirikit National Institute of Child Health from February to June 2000. History taking, weight-height measurement, and blood testing for complete blood count (CBC) and serum folate level were done. Patients were randomly by assigned into 2 groups. The study group was supplemented daily with multivitamins (MVD) along with a folic acid tablet while the control group was supplemented daily with MVD only, for 6 weeks.

Results : Twenty-nine malnourished children were enrolled in the present study. They were randomly by assigned into 2 groups, 14 children in the study group and 15 children in the control group. There were 11 boys (38%) and 18 girls (62%). Mean age was 36.3 months. Anemia and low serum folate level were found in 24 per cent and 21 per cent respectively. There was no significant difference in the data of both groups, except that anemia was more common in the study group ($p = 0.018$).

After 6 weeks of supplementation, increases in weight and serum folate level were significantly higher in the study group, but there was no significant difference in weight increased between both groups.

Conclusion : Folate deficiency may be found in malnourished children. Efficacy of folic acid supplement is good. Folic acid needs to be supplemented in malnourished children.

Key word : Multivitamins, Folate, Malnutrition, Children

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Malnutrition is an important public health problem, especially during childhood[1]. It effects growth, development and immunity in children. Malnourished children are very susceptible to infection and its complications, leading to high morbidity and mortality[1]. Many micronutrient deficiencies such as vitamins and minerals are associated with protein and energy malnutrition[1]. Nutrient deficiencies always present sub-clinically before presenting with clinical manifestations[2]. Laboratory tests are needed to diagnose these sub-clinical deficiencies[2]. Folate is a water-soluble vitamin in the vitamin B group. It has a key role in DNA synthesis and assists in the renewal of epithelial cells by accelerating the normal regeneration of damaged cells[3]. Folic acid deficiency worldwide coexists with poverty, malnutrition and infections. Folic acid deficiency is diagnosed by low serum or red blood cell (RBC) folate after no folate intake for 2 weeks[4]. Folate deficiency may lead to an impairment of both cell-mediated and humoral immunity. Many children refuse to eat leafy vegetables, a good source of folate. Supplementation of multivitamins in malnourished children is recommended, but some multivitamin preparations do not contain folic acid. Folic acid is synthetic, heat stable, and twice as bioavailable as the folate[5]. In the present study it was hypothesized that multivitamin-supplementation with folic acid would have a positive effect on weight gain and serum folate in malnourished children.

SUBJECTS AND METHOD

Twenty-nine malnourished children attending the Nutrition Clinic at Queen Sirikit National Institute of Child Health (QSNICH) were prospectively studied from February to June 2000. The children were randomly assigned into 2 groups. Fourteen children of the study group were daily supplemented with 1 ml of multivitamin drop (MVD) along with a folic acid tablet (5 mg) and the control group was daily supplemented only with 1 ml of MVD. Composition of MVD is shown in Table 1.

Excluded from the study were those malnourished children, who had

1. been on vitamins in the previous 4 months before enrollment.
2. an underlying disease.
3. been ill a week before enrollment.
4. lost follow-up from the study.
5. refused the supplement.

The definition of malnutrition was described by using Thai Growth Reference (1999) as follows[1, 2],

Underweight	%weight for age (%W/A) $\leq$ 90
Wasting	%weight for height (%W/H) $\leq$ 90
Stunting	%height for age (%H/A) $\leq$ 95

Parents signed an informed consent form and history was obtained by parental interview. Then a physical examination, including weight and height measurement and blood samples were drawn from each child. Blood samples were sent to the hematological laboratory for complete blood count (CBC), and to the Department of Tropical Medicine, Mahidol University for serum folate levels. Hemoglobin (Hb) level less than 11 g per cent was defined as anemia and serum folate levels less than 5 ng/ml was defined as low. All parents received nutrition education from the investigating physician and dietician.

Parents received prescriptions of MVD and folic acid tablets for their children. Children were followed-up every 3 weeks for 6 week duration, when weight was recorded and physical examination was performed. A pharmacist checked compliance by interview at each visit, before giving a new prescription. After 6 weeks, a blood sample was drawn for serum folate level.

Analysis

Data was analyzed into mean and standard deviation (SD). Comparison between groups was done using Chi-square, Fisher Extract and unpaired *t*-test. Comparison within each group was done with paired *t*-test. P-value less than 0.05, was considered statistically significant.

RESULT

Twenty-nine malnourished children were included in the present study. They were 38 per cent male, and 62 per cent female randomly assigned into 2 groups, as the study group (14) and the control group (15) (Table 2). Ages ranged between 8-68 months with a mean age of 36.3 months. The baseline data such as sex, nutritional status, and history of no-vegetable intake were not different between the two groups. Mean values of nutritional indices and serum folate were not different between the 2 groups, except that the mean hemoglobin level in the study group was significantly lower than the control group (Table 3). The prevalence of anemia was significantly higher in the study group (Table 2). Red blood cell (RBC) morphology was found as normocytic 75 per cent and microcytic 25 per cent. Low serum folate level was found in 6 cases with an equal number in both groups.

Table 1. Compositions in each ml of MVD and recommended daily allowance (RDA).

Vitamins	A (μg)	D (μg)	C (mg)	B1 (mg)	B2 (mg)	B6 (mg)	Niacin (mg)	Folate (μg)	B12 (μg)
MVD 1 ml	600	10	40	2	2	1.8	15	-	5
RDA									
0-1 year	375	7.5-10	30-35	0.3-0.4	0.4-0.5	0.3-0.6	5-6	25-35	0.3-0.5
1-10 years	400-700	10	40-45	0.7-1	0.8-1.2	1-1.4	9-13	50-100	0.7-1.4

Table 2. Number of children according to sex, nutritional status, history and blood testing.

Related factors	Study group (14)	%	Control group (15)	%	P-value	Total (29)	%
Male	3		8		0.16	11	37.9
Female	11		7			18	62.1
Underweight	14	100	14	93.3	0.52	28	96.6
Wasting	13	92.9	12	80	0.59	25	86.2
Stunting	7	50	6	40	0.86	13	44.8
History of no-vegetable intake	7	50	4	26.7	0.36	11	37.9
Anemia	6	42.9	1	6.7	0.035	7	24.1
Low serum folate	3	21.4	3	20	0.64	6	20.7

Table 3. Mean ± SD of age, nutritional status, hemoglobin and serum folic acid.

Mean ± SD	Study group (14)	Control group (15)	P-value
Age (month)	38.7 ± 22.5	34 ± 17.4	0.6
%W/A	76.5 ± 4.3	78.2 ± 8.2	0.39
%H/A	94.3 ± 1.8	95.6 ± 5.2	0.42
%W/H	85.9 ± 5.1	85.6 ± 4.9	0.92
Hemoglobin (g%)	11.0 ± 1.2	11.9 ± 0.8	0.03
Serum folate (ng/ml) - 1st	13.0 ± 8.7	14.2 ± 9.7	0.59

There was no correlation among the low serum folate level, sex and history of non-vegetable intake (Table 4).

After supplementation for 6 weeks, both groups had gained weight at an average of 403 ± 560 grams. Weight gain was not different between the 2 groups, but it increased significantly in each group with normal serum folate level (Table 5, 6). Mean serum folate increase was 7.9 ± 12.9 ng/ml. Increased serum folate was significant in the study group. Folate deficiency was still found in 3 cases of the control group.

DISCUSSION

Folic acid affects growth, development and immunity in children[3,6]. Malnutrition plays a role in the development of folate deficiencies[7]. Folate deficiency in the present study was found in 21 per cent with no difference between the sexes. This prevalence of folate deficiency was higher than other adult studies, such as 6.9 per cent in male workers at a Thai construction site in urban Bangkok[8] and 4.3 per cent in rural women of child bearing age in northeastern Thailand[9]. Malnourished children are at high risk for the development of folate deficiency as reported

Table 4. History of non-vegetable intake and sex in relation to serum folate level.

Serum folate level	Low serum folate (6)	Normal serum folate (23)	P-value
History of no-vegetable intake: no/yes	2/4	9/14	0.59
Male/female	4/2	7/16	0.16

Table 5. Changes in weight and serum folate level after supplementation.

Mean ± SD	Study group (14)	Control group (15)	P-value
Increased weight (kg)	0.46 ± 0.52	0.41 ± 0.62	0.79
Serum folate (ng/ml) - 2nd	27.8 ± 13.5	14.1 ± 9.2	0.003
Increased serum folate (ng/ml)	15.5 ± 11.4	-0.161 ± 8.7	0.0002

Table 6. Mean ± SD of weight and serum folate level before and after 6 weeks of supplementation.

Mean ± SD	Study group (14)			Control group (15)		
	Before	After	P value	Before	After	P value
Weight (kg)	10.5 ± 2.9	10.9 ± 2.9	0.028	10.5 ± 2.7	10.9 ± 2.8	0.096
Serum folate (ng/ml)	13.0 ± 8.7	29.7 ± 11.8	0.001	14.2 ± 9.7	14.1 ± 9.2	0.908
Previous low Serum folate						
Weight (kg)	10.6 ± 2.9	11.1 ± 2.9	0.25	10.9 ± 1.5	11 ± 1.3	0.55
Serum folate (ng/ml)	3.7 ± 0.3	28.1 ± 4.0	0.009	3.0 ± 0.9	4.8 ± 2.3	0.19
Previous normal Serum folate						
Weight (kg)	10.5 ± 3.1	10.9 ± 3.0	0.022	10.4 ± 2.9	10.8 ± 3.1	0.03
Serum folate (ng/ml)	15.6 ± 8.1	30.2 ± 13.2	0.002	17.1 ± 8.7	16.4 ± 8.9	0.82

in community studies[4,7]. Low serum folate in the present study was not associated with megaloblastic anemia. Serum folate is an indicator of dietary folate, low level indicates a negative folate balance, and RBC folate reflects storage in the tissues or reserve of the body[11,12]. The diagnosis of megaloblastic anemia requires clinical manifestations and other laboratory evaluations apart from serum folate level[10,13]. Nutrient deficiencies always present sub-clinically so laboratory tests are needed to diagnose these sub-clinical deficiencies[2,3]. In the present study, 18 children had a history of no-vegetable intake but only 4 children (22%) had a low serum folate level. Fresh green vegetables, yeast and organ meats are good sources of folate[3]. These young children were usually fed with liver, egg, meat, and fortified milk, a good alternative source of folate. At 6 weeks, formula-fed infants had significantly higher folate intakes and blood concentrations[14]. Two children, who had a history of vegetable intake, had low serum folate. Bio-availability of folate is 50-70 per cent, and overboiling, as is the norm in preparation of baby foods, destroys folate[3,6,15]. During the childhood period of rapid growth, folic acid requirement increases[3]. Serum folate increased significantly in the study group, averaging 15.5 ± 11.4 ng/ml after folic acid supplementation was given for 6 weeks in each child, not dependent on previous serum folate levels. Three cases in the control group still had folate deficiency. A study has shown that serum folate significantly increased for up to 6 h after intake of spinach and folic acid[16]. Also serum folate levels have shown linear

increases of 5.5 nmol/l or 2.43 ng/ml for every 0.1 mg of folic acid, which is higher than that seen in the present study[17]. After folic acid supplementation, weight increased significantly in the groups with normal serum folate. Intakes of folic acid up to 5 mg/day have not shown any adverse effect[4,18]. In the study group, cases with low serum folate did not have significant weight gain, even though they were supplemented with multivitamins. But cases with normal serum folate level resulted in significant weight gain after multivitamin supplementation only. A previous study showed that in a supplemented group of infants, weight and length attained at 6 months and rate of gain were higher in infants whose folate levels were above the median value[19]. In malnourished children many micronutrient deficiencies such as folate deficiency were found[1,4]. So supplementation to replace the deficit is necessary.

SUMMARY

Multivitamins need to be supplemented in malnourished children and also folic acid, especially in cases with a history of no-vegetable intake.

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ผลของการเสริมวิตามินรวมและยาเม็ดโฟเลตในเด็กที่มีปัญหาทุโภชนาการ

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วัตถุประสงค์ : ศึกษาผลของการเสริมวิตามินรวมและยาเม็ดโฟเลตต่อระดับโฟเลตในเลือดและการเพิ่มของน้ำหนัก

วัสดุและวิธีการ : เป็นการศึกษาแบบ Prospective randomized controlled study ในเด็กที่มีภาวะทุโภชนาการที่มารักษาในคลินิกโภชนาการ สถาบันสุขภาพเด็กแห่งชาติมหาราชินี ระหว่างเดือนกุมภาพันธ์–มิถุนายน พ.ศ. 2543 แบ่งเด็กเป็น 2 กลุ่มโดยการสุ่ม กลุ่มศึกษาจะได้รับวิตามินรวมร่วมกับยาเม็ดกรดโฟลิคทุกวัน และกลุ่มควบคุมจะได้รับเฉพาะวิตามินรวมทุกวัน เป็นเวลา 6 สัปดาห์

การวัดผลหลัก : การเพิ่มขึ้นของน้ำหนักและระดับโฟเลตในเลือด

ผล : ศึกษาเด็กที่มีภาวะทุโภชนาการจำนวน 29 คน อายุระหว่าง 8 เดือน–5 ปี 10 เดือน เป็นเพศชายร้อยละ 38 และหญิงร้อยละ 62 อายุเฉลี่ย 36.3 เดือน แบ่งเป็น 2 กลุ่ม คือ กลุ่มศึกษา 14 คนและกลุ่มควบคุม 15 คน ภาวะซีดและระดับโฟเลตในเลือดต่ำพบร้อยละ 24 และ 21 ตามลำดับ ไม่พบความแตกต่างในข้อมูลระหว่าง 2 กลุ่ม ยกเว้นในกลุ่มศึกษาพบภาวะซีดสูงกว่าอย่างมีนัยสำคัญทางสถิติ หลังการเสริมยาวิตามินรวมและยาเม็ดโฟเลต 6 สัปดาห์ พบว่ากลุ่มศึกษามีน้ำหนักตัวและระดับโฟเลตเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ แต่เปรียบเทียบการเพิ่มขึ้นของน้ำหนักระหว่างกลุ่มไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ

สรุป : การขาดสารโฟเลตอาจพบได้ในภาวะทุโภชนาการ ผลของการเสริมด้วยกรดโฟลิคมีประสิทธิภาพดี การเสริมวิตามินรวมชนิดที่มีสารโฟเลตให้แก่เด็กที่มีภาวะทุโภชนาการเป็นสิ่งจำเป็น

คำสำคัญ : วิตามินรวม, โฟเลต, ภาวะทุโภชนาการ, เด็ก

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