Assessment of protein-energy malnutrition in children with chronic arthritis

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Protein-energy malnutrition (PEM) has been estimated to occur in 10 to 50% of children with juvenile chronic arthritis (JCA). Thirty-eight children with JCA were evaluated and their nutritional status determined, and they were compared with 23 healthy sex and age-matched children as controls. A standardized, 9-parameter comprehensive nutritional assessment profile was used. The simple anthropometric measurements, height and weight for age, were abnormal in 30% and 27% of the patients, respectively. A detailed evaluation revealed that 71% had abnormal somatic protein stores, and that they also had significantly low levels of visceral protein stores, when compared to their healthy peers. The results were consistent with the fact that inflammation put the JCA patients at significant risk for developing complicated malnutrition and it might result in PEM without any obvious signs of malnutrition. A nutritional screening test would be very useful in detecting early PEM in children with chronic arthritis.

Key words: PEM, chronic arthritis.

It is well known that many children with chronic diseases are poorly nourished; this is no less true for children with chronic arthritis. Protein-energy malnutrition (PEM) has been estimated to occur in 10 to 50% of children with juvenile chronic arthritis (JCA)[1]. Children with active JCA are often anorexic, and in one study, their dietary intake was only three-quarters of the recommended dietary allowance for age[2].

When a child is determined to be at risk of becoming nutritionally depleted, precipitating factors such as inadequate intake, reduced absorption, excessive losses, impaired utilization, or increased requirements must be established. Accurate assessment of a child's nutritional status is an important element of pediatric care. Successful nutritional assessment is predicated on an awareness of nutritional deficiencies secondary to other processes: disease states and drug therapies that precipitate specific nutrient depletion[3]. In this study, JCA patients were evaluated, their nutritional status was determined and they were compared with a healthy sex-and age-matched control group.

Material and Methods

Thirty-eight children with JCA who were followed up in the Pediatric Rheumatology Unit were included in the study. They all satisfied the American College of Rheumatology (ACR)[4] and European League Against Rheumatism (EULAR)[5] criteria for JCA. Twenty-three healthy, age-and sex-matched subjects were selected as a control group. Twenty-one (55%) of the patients were receiving naproxen sodium, and 17 (45%) were receiving steroid + weekly oral methotrexate (10 mg/m^2/wk). All the patients receiving steroid therapy were on prednisone at the beginning, which was then switched to deflazacort during the low-dose regimen. The JCA patient was considered in "partial remission" when he received medication and had mild or no joint symptoms and the examination revealed minimal evidence of active disease, and "active" when there were persistent joint symptoms and physical evidence of active joint inflammation, despite receiving medication.

All children in the study were evaluated by the Pediatric Nutrition and Metabolism Unit. A Harpenden stadiometer and a Seca beam balance

scale were used to measure height and weight, respectively. A Holtain Ltd., Crymrch (UK) caliper was used to measure triceps skinfold thickness (tsf) (three times) at the midpoint between the acromion and the olecranon process, and the three measurements were averaged. Mid-arm circumference (mac) was measured at the same point and arm muscle area (ama) was calculated as: ama=[mac(cm)-0.314 x tsf (mm)]^2/12.56.

Anthropometrical parameters were expressed as percent of standard, i.e., the median value of the age-and sex-matched reference population. National Center for Health Statistics data was used for standard values[6]. Serum albumin and iron binding capacity were measured by conventional methods. Serum transferrin was calculated as transferrin = [0.8 x total iron binding capacity (TIBC)-43]. Serum prealbumin (PAB) and serum retinol binding protein (RBP) were assessed by radial immunodiffusion technique. Creatinine-height index (CHI) was calculated as CHI=(actual urinary creatinine/ ideal urinary creatinine) x 100. Table I shows the nutritional assessment parameters which are indicators of protein-energy malnutrition. Mann-Whitney U test was used for statistical analysis for comparison of the groups, and p values below 0.05 were regarded as significant.

Table I. Nutritional Assessment Parameters for Determining Protein-Energy Malnutrition

Nutritional parameter	Abnormal value		
Height for age	< 95%		
Weight for height index	< 90%		
Triceps skinfold thickness	< 90%		
Arm muscle area	< 90%		
Serum albumin	< 3.5 g/dl		
Serum prealbumin	< 5th percentile		
Serum retional binding protein	for adjusted norms		
Serum transferrin	< 200 mg/dl		
Creatinine-height index	severe < 40%	moderate 40%-60%	mild 60%-80%

Results

The patient and control groups were classified according to sex and age, and disease subgroups, duration, activity and the medications used were recorded (Table II). The mean age of the patients was 10.6 years (3.0-17.0 years), and of the control group 10.3 years (3.0-16.0 years). Forty-two percent were female and 58% were male in the JCA group, and 48% were female and 52% were male for healthy controls. The mean duration of JCA was 3.3 years (1-14 years). Disease onset was systemic in nine (24%), polyarticular in 20 (52%), and oligoarticular in nine (24%) patients; the course was systemic in two (5%), polyarticular in 20 (52%), and oligoarticular in 16 (43%). The number of patients receiving steroid therapy at the time of nutritional evaluation or during the preceding six months was 38 (36%), 35 (92%) were on low dose, and 3 (8%) were on high dose. At the time of the evaluation, 30 (79%) patients were noted to be in partial remission, and eight (21%) had active disease. Nutritional comparison of patients and controls is shown in Table III. It consists of three main parts: the first two columns compare the patients and controls. Patients' height for age, arm muscle area, serum prealbumin, retinol binding protein and transferrin levels were found to be significantly lower than those of the controls ($p < 0.05$). Patients with active disease and those in partial remission are compared in the third and fourth columns. Serum prealbumin, retinol binding protein and transferrin levels were found to be significantly lower in the active disease group ($p < 0.05$). There was no significant difference between the patients receiving naproxen versus methotrexate + deflazacort (MTX + DFC) by means of nutritional status, as defined in the fifth and sixth columns, respectively. Table IV compares the patient and control groups according to the abnormal nutritional parameters. Forty-two percent of the patients' height for age was under 95%; it was 7% for the control group ($p < 0.05$). Weight for height index was under 90% in 29% of patients, whereas all the controls were in the normal range ($p < 0.05$). Arm muscle area was under 90% in 71% of patients and in 31% of the control group ($p < 0.05$). None of the patients' serum transferrin levels was below 200 mg/dl, whereas levels were below 200 mg/dl in 39% of the controls ($p < 0.05$). Creatinine-height index was abnormal in 18% of patients and in none of the controls ($p < 0.05$). Height for age, weight for height index, arm muscle area, serum transferrin level and creatinine-height index were significantly lower in the patients with active disease than in those in partial remission. Height for age, serum albumin and transferrin levels and creatinine-height index were significantly lower in patients on MTX + DFC, when compared with those taking only naproxen.

Table II. Demographics and Patient Characteristics

		Patients (n = 38)		Control group (n = 23)		
Sex (F/M)		16/22		11/12		
Age at time of study (yrs)	mean 10.6	median 10.5	range 3-17	mean 10.3	median 10.0	range 3-16
Age at disease onset	mean 6.6	median 6.0	range 0.5-15			
Disease duration (yrs)	mean 3.3	median 2.0	range 1-14			
Partial remission/active disease		30/8 (79% - 21%)				
JCA subtype	Systemic	Polyarticular	Oligoarticular			
Onset	9 (24%)	20 (52%)	9 (24%)			
Course	2 (5%)	20 (52%)	16 (43%)			
Medications		Naproxen 21 (55%)	MTX+DFC[1] 17 (45%)			
Steroid therapy Patients receiving at the time of study or during preceding 6 months n = 14 (36%)						
Steroid dose (mg/kg/d)[2]		low 35 (92%)	high 3 (8%)			

1: Methotrexate (10 mg/m2/wk) + low-dose deflazacort.
2: Low dose = 0.5 mg/kg/d equivalent dose for prednisone.
High dose = 1-2 mg/kg/d prednisone.
JCA: juvenile chronic arthritis.

Table III. Nutritional Comparison of Patients and Controls, Patients With Active Disease and Those in Partial Remission, and Patients Receiving Naproxen Versus MTX + DFC

Parameter	Patients n=38	Controls n=23	Active disease n=8	Partial remission n=30	naproxen n=21	MTX + DFC* n=17
Height for age (% std)	99.8 ± 18.7[1] (69.2-183.8)	10.4.4 ± 5.5[1] (95.3-113.1)	90.3 ± 12.5 (69.2-108.9)	102.4 ± 19.4 (88.9-183.8)	104.5 ± 22.9 (85.5-183.8)	94.0 ± 9.4 (69.2-108.9)
Weight for height index (% std)	103.4 ± 17.5 (77.7-147.7)	101.2 ± 12.8 (87.0-137.2)	107.4 ± 20.9 (87.5-147.7)	102.0 ± 16.9 (77.7-147.7)	101.3 ± 13.7 (80.9-135.0)	106.7 ± 20.9 (77.7-147.7)
Triceps skinfold (% std)	108.7 ± 35.8 (12.0-150.0)	120.1 ± 25.3 (76.5-150)	102 ± 43.4 (45.0-150.0)	102.4 ± 27.4 (43.5-150.0)	103.7 ± 29.9 (58.5-150.0)	114.2 ± 47.6 (12.0-150.0)
Arm muscle area (% std)	81.6 ± 25.9[2] (40.5-150.0)	96.7 ± 12.2[2] (69.0-130.0)	77.3 ± 24.2 (46.5-126.0)	81.2 ± 23.7 (40.5-150.0)	83.1 ± 28.1 (40.5-150.0)	83.3 ± 29.0 (45.0-150.0)
Serum albumin (g/dl)	3.9 ± 0.5 (2.3-4.6)	4.1 ± 0.3 (3.6-4.6)	4.1 ± 0.2 (3.8-4.3)	3.9 ± 0.6 (2.3-4.6)	4.1 ± 0.5 (2.6-4.6)	3.9 ± 0.6 (2.3-5.0)
Serum prealbumin (mg/L)	172.8 ± 51.3[3] (69.0-299.6)	245.4 ± 56.1[3] (162.9-337)	178 ± 47.6[6] (69.0-270.0)	210.3 ± 53.5[6] (156.2-310.6)	188.2 ± 55.6 (89.1-299.6)	179.0 ± 54.5 (69.0-268.5)
Serum retinol binding protein (mg/dl)	34.5 ± 6.4[4] (19.4-46.0)	44.4 ± 8.8[4] (29.6-55.8)	35.4 ± 5.9[7] (19.4-39.0)	42.0 ± 6.6[7] (27.2-46.0)	35.6 ± 5.9 (20.1-46.0)	35.1 ± 6.2 (19.4-42.2)
Serum transferrin (mg/dl)	204.0 ± 25.4[5] (165.0-274.0)	236.8 ± 44.0[3] (139.0-299.0)	227.9 ± 45.2[8] (139.0-299.0)	271.3 ± 15.08 (245.0-291.0)	248.1 ± 41.1 (139.0-299.0)	228.0 ± 45.9 (157.0-299.0)
Creatinine-height index (% std)	124 ± 37.9 (22.5-150.0)	137.6 ± 19.6 (84.0-150.0)	131.8 ± 34.4 (245.0-291.0)	122.1 ± 39.0 (22.5-150.0)	128.6 ± 37.2 (22.5-150.0)	118.6 ± 39.1 (51.0-150.0)

*: Methotrexate (10 mg/m2/wk) + low-dose deflazacort.
1-8: $p < 0.05$ (Mann-Whitney U-Wilcoxon rank sum W test).

Table IV. Comparison of Patients and Controls, Patients With Active Disease and Those in Partial Remission, and Patients Receiving Naproxen Versus MTX + DFC Using the Nutritional Assessment Parameters Which Are Indicators of Protein-Energy Malnutrition

Abnormal parameter	Patients n=38	Controls n=23	Active disease n=8	Partial remission n=30	naproxen n=21	MTX + DFC* n=17
Height for age (< 95%)	16 (42%)[1]	1 (7%)[1]	6 (75%)[6]	10 (33%)[6]	6 (29%)[11]	10 (59%)[11]
Weight for height index (< 90%)	11 (29%)[2]	none[2]	2 (25%)[7]	9 (30%)[7]	6 (29%)	5 (29%)
Triceps skinfold (< 90%)	11 (29%)	2 (15%)	3 (38%)	8 (27%)	6 (29%)	5 (29%)
Arm muscle area (< 90%)	27 (71%)[3]	4 (31%)[3]	7 (88%)[8]	20 (67%)[8]	15 (71%)	12 (71%)
Serum albumin (< 3.5 g/dl)	3 (8%)	none	1 (13%)	2 (7%)	none[12]	3 (18%)[12]
Serum transferrin (< 200 mg/dl)	9 (39%)[4]	none[4]	10 (33%)[9]	none[9]	2 (12%)[13]	6 (29%)[13]
Creatinine-height index (abnormal)	7 (18%)[5]	none[5]	5 (63%)[10]	2 (7%)[10]	2 (10%)[14]	5 (24%)[14]

*: Methotrexate (10 mg/m²/wk) + low-dose deflazacort.
1-4: $p < 0.05$ (chi-square test).

Discussion

A number of factors contribute to decreased food intake in children with JCA. Inflammatory mediators such as interleukin-1 and tumour necrosis factor are increased and they have been shown to cause anorexia[7,8,9]. The roles of interleukin-6 and the aforementioned clearly demonstrate a correlation between growth delay and JCA[10,11]. Recent studies indicating the role of adhesion molecules in JCA have focused on circulating levels of soluble E-selection (sE-selection), P-selection and intercellular adhesion molecule-1 (sICAM-1) in patients with JCA, and it was found that levels of sE-selection and sICAM-1 were significantly correlated with levels of soluble TNF receptor 2, especially in systemic arthritis[12]. Another important factor, fever, could contribute to the increased nutrient requirements in these patients. Children experiencing depression or severe pain because of their disease also become anorexic. In some families, socioeconomic factors might prevent families from purchasing adequate nourishment for their children. So, it is unlikely that growth retardation is due solely to steroid use[2]. In this study, we used a standardized, 9-parameter comprehensive nutritional assessment profile, and compared the patients with sex-and age-matched healthy controls. In a study done by Bernstein et al.[13], they found that 33% of children with JCA had heights below the 3rd percentile, and the ratio had increased to 53% after 7.5 years. In this study, the results were similar and 30% and 27% of the patients had heights and weights under the 3rd percentile, respectively. Henderson and Lovell[14] found that only 30% of patients with PEM had heights under the 5th percentile, but 90% of them had subnormal somatic protein stores, as measured by arm circumference, and arm muscle circumference and area. Thus, a detailed nutritional assessment was able to document more accurate data in these children, mostly by including the ones with mild PEM. We found a significant difference between the patients and sex-age matched control, in terms of arm muscle area. We also determined the levels of visceral protein stores (serum albumin, PAB and RBP) and also serum transferrin, as we knew they would be the early predictors of PEM. We agree that the significantly low levels of PAB and RBP in our patients, consistent with the results of Henderson and Lovell[14], support the interpretation that they result primarily from poor nutrition rather than from inflammation. Another important point is that when malnutrition is complicated by inflammation, weight loss tends to come from lean body mass such as skeletal muscle, rather than from fat[15-17]. Our results are also consistent with the fact that inflammation puts these patients at significant risk of developing complicated malnutrition and may result in PEM without any obvious signs of malnutrition. In a study from Kirel et al.[18], serum iron levels and transferrin saturation were low in all JCA patients, and there was a significant correlation between ferritin levels and C-reactive (CRP) and Erythrocyte sedimentation rate (ESR) indicating the disease activity. We found a significant difference between the visceral protein stores in patients and in the healthy control group, whereas there was no statistical difference in their subcutaneous fat stores, as also documented by Henderson and Lovell[14]. Henderson et al.[19] also proposed a nutritional

screening test with a sensitivity and specificity of 80% and 86%, respectively. We strongly support the use of this test in rheumatology clinics in order to document many JCA patients who may have undiagnosed mild PEM. Regarding the multidisciplinary evaluation of patients with JCA, there is a need for involvement of the pediatric Nutrition and Metabolism Unit to facilitate early recognition of potential nutritional problems in this population.

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