

Gluten-Free Diet in Juvenile Idiopathic Arthritis

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Abstract

Aim: Gluten-free diet may attenuate joint symptoms in adult rheumatoid arthritis. We conducted a groundwork study on the effect of a gluten-free diet in children with arthritis.

Methods: 4 children (aged 5-12) with juvenile idiopathic arthritis (JIA) were recruited for a study including 3 months on a gluten-free diet. Articular symptoms and signs, and the presence of antibodies to gliadin, endomysium, transglutaminase, and milk were determined at 0, 3, and 6 months as well as immunoglobulins, blood count, ESR, CRP and markers for intestinal inflammation, alpha-1-antitrypsin, physician's and patient's VAS, a CHAQ-form, and JADAS10.

Results: In a 5-year old boy articular and gastrointestinal symptoms improved during gluten-free diet. A 12-year old girl experienced some relief and disease activity scores showed moderate improvement. In two other patients the objective measurements were unaltered. In one of these two, antigliadin-IgG and milk-IgA antibodies remained elevated throughout the study.

Conclusions: Results of this small prospective study on gluten free diet in patients with JIA were inconclusive although some subjective improvement was observed. A more extensive study including patients with more active disease seems warranted.

Keywords: Gluten; Free diet; JIA; Diet manipulation

Introduction

Patients and their families are frequently concerned whether their diet might effect on the symptoms of juvenile idiopathic arthritis (JIA). There are, however, limited data on the effect of dietary manipulation on the disease activity in JIA. In the 1990's some reports related to arthritis focused on e.g. zinc, copper and alpha-linolenic acid intake [1,2] but during the last few years there have been fewer studies on dietary matters.

In adults, most dietary studies have been conducted in patients with rheumatoid arthritis; the focus has been on vegan diets [3]. A study by Hafström et al. showed that a vegan diet free of gluten relieved the joint symptoms in adult patients [4]. In those who responded to the dietary modification, serum levels of antigliadin antibodies declined suggesting a reduction in immunoreactivity to food antigens [4]. There are few reports stating that a gluten-free diet may diminish joint symptoms in adult patients with rheumatoid arthritis [3] and other reports contradicting the effect of this diet modification [5]. The extensive, recent Cochrane review of the dietary effects in rheumatoid arthritis in adults shows systematically how difficult these studies are to conduct and how the level of evidence of benefits of different kinds of diets is likely to be modest [6]. A recent study in adults with chronic arthritis demonstrated potential anti-inflammatory and atheroprotective effects of gluten-free diet [7]. Further, in a study on psoriasis 16% of the patients were shown to have IgA/IgG antibodies to gliadin and gluten-free diet appeared to relieve the disease activity measured by PASI-index. None of these patients had antiendomysium antibodies, thus overt coeliac disease was unlikely [8]. Antigliadin antibodies are also frequent findings in JIA [9,10] suggesting intestinal irritation in these patients but only little is known about dietary modifications in juvenile idiopathic arthritis (JIA).

Many families are troubled with the diverse information flooding from various sources in relation to diet and are prone to modify child's diet which may potentially be harmful [11]. Thus, it would be supportive to investigate dietary effects on childhood autoimmune diseases as the families often consider this as a key issue. This preliminary work was designed to study the effect of a gluten-free diet on the symptoms of

children with JIA, the idea for the study coming from families wishing to try dietary modifications, mainly gluten-free diet.

Patients and Methods

Subjects introduced to dietary modification

Six JIA patients (age 5 to 12 years) and their families visiting the Rheumatology unit of the Department of Pediatrics, University Central Hospital, Helsinki, Finland expressed their desire to try gluten free diet. Once the required diet modifications were explained, 4 families out of 6 candidates agreed to join this preliminary follow-up diet study. Two families considered the modifications too complicated. All four children joining the study had juvenile polyarthritis according to the ILAR criteria [12]. The diagnosis of JIA had been settled within 20 months in three patients and 44 months earlier in one patient. All patients included in the study were older than four years at the time of diagnosis. They all were on systemic methotrexate treatment (10-15 mg/m²) together with folate substitution (5 mg weekly) since 6-13 months before inclusion. None of them were on systemic corticosteroid treatment or had intra-articular corticosteroid injections during the study period. All four children used NSAIDs on irregular basis.

The clinical characteristics of the children are shown in Table 1. The presence of HLA B27 and serum antinuclear antibodies (S-ANA) were determined at the time of diagnosis. None of these children had a diagnosis of food allergy and each child tolerated milk but they all had recurrent abdominal pain before entering the study, the stomach ache not directly correlating to the NSAID usage.

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Laboratory tests including determinations of serum IgA antibodies to endomysium and tissue transglutaminase, anti gliadin antibodies of IgA and IgG class, IgA antibodies to milk, serum immunoglobulins (IgG, IgA, IgM), complete blood cell count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), and alpha-1-antitrypsin concentration were performed at the clinical laboratory at screening, after three months on a mixed (no food restrictions and wheat allowed) diet and again after three months on a gluten-free diet.

A nutritional therapist advised the families for the diets. The families completed detailed dietary records for three days prior to the follow-up visits according to the food diary routine at our clinics. At each visit, the compliance was discussed.

Articular symptoms and signs were evaluated clinically at 0, 3 and 6 months by one of the authors (KA) as well as global assessment of the disease activity by visual analogue scale (doctor's VAS, 0 -100). The patients or families filled in a Childhood Health Assessment Questionnaire (CHAQ)-form that has been validated for clinical use to assess physical functioning (score 0-3) [13]. The assessment of global well-being of the patient was judged by parents using the visual analogue scale (patient's VAS, 0 -100) [13]. JADAS10, a new tool for paediatric JIA patients resembling DAS for adult patients [14,15] was used to get more information on the disease (arthritis) activity. In JADAS10 (range 0-40) the parameters comprise the physician's global assessment (VAS), the parent's/patient's global assessment (VAS), the normalized ESR (Δ ESR) and the 10-joint reduced count (10 joints are included). The value of 2.0 is proposed cut-point for remission and value 2.9 for minimal disease activity in polyarthritis [16].

Results

In two of the four patients (Patient 1 and 2), objective measurements of the disease activity showed some improvement (Table 2). In the remaining two patients, no clear effect in the measurements of the disease activity was noticed (Table 2). In patient 1, the mother and the child himself felt that articular and particularly gastrointestinal symptoms improved on a gluten-free diet (Table 1). Likewise, patient 3 experienced subjective improvement of GI-symptoms (Table 1). In three patients JADAS10 values showed that the patients were either in remission or had a low disease activity.

Serum IgA antibodies to endomysium and transglutaminase were within the normal range in all children throughout the study. There were no changes in serum levels of CRP, which were all within normal range (<10 mg/l) or in fecal alpha-1-antitrypsin concentrations (all normal values <200 µg/g). Likewise, the serum levels of Hb and serum IgG, IgA, and IgM were within normal ranges for age (data not shown). Two children had elevated IgA antibodies to milk (Table 3). Of these two, one had elevated anti gliadin-IgG antibodies.

Discussion

Anti gliadin antibodies are frequently encountered in JIA [9,10] most likely reflecting non-specific immune stimulation [9,10]. One patient in the present study had an increased level of anti gliadin antibodies of IgG class. This was considered as an unspecific finding as the specific screening tests for coeliac disease, antiendomysium and anti-transglutaminase IgA antibodies, were within the normal range. Unexpectedly, during a gluten-free diet, the antibodies remained elevated. This particular child had also constantly elevated milk IgA antibodies but tolerated cow's milk well. She experienced some subjective relief during a gluten-free diet but objective measurements on the JIA activity improved only to some extent. Though all the

patients had polyarthritis, only one patient was HLA B27 positive and S-ANA negative suggesting a different type of disease pathogenesis from the other three patients, but not yet fulfilling the criteria of spondylarthropathy. This patient also had constantly elevated milk IgA antibodies suggesting gut irritation although she tolerated milk and her fecal alpha-1-antitrypsin content remained low.

Gut epithelium protects an individual from harmful antigens and loss of this integrity may lead to a substantial increase in the antigenic load of the body. Subsequently, disruption in the gut epithelium and a change in antigenic challenge may influence the degree of joint inflammation in patients with rheumatoid arthritis as has been suggested [17]. In spondylarthropathies, the remission of the joint inflammation is associated with the healing of gut inflammation [18]. In JIA gut permeability may be increased [19] and fecal alpha-1-antitrypsin is frequently elevated reflecting gastrointestinal involvement [20]. On the other hand, in disorders of the gut such as coeliac disease, arthritis may be the first manifestation of an untreated disease. When coeliac patients are introduced to a gluten-free diet their joint symptoms disappear [3].

Dietary assessments are difficult to conduct, especially in disorders with wide fluctuations in disease activity. The compliance can be poor, and the monitoring of the diet is tedious [21]. In our study, a nutrition therapist advised on the diets prior to the introduction of a gluten-free diet. The families and patients had a high motivation for this trial and their adherence to the gluten-free diet was considered sufficient according to the detailed dietary records that the families filled in prior to the control visits (data not shown). The families argued, however, that the gluten-free diet was difficult to follow. All the families wanted to revert back to the normal diet without any food restrictions after the study except for the family in which the gluten-free diet seemed to relieve articular and abdominal symptoms of the child.

In an open study, the positive expectations of the patients or physicians are likely to cause bias in the results. In our study, the subjective view of the articular disease activity was assessed with validated forms [13-15] and the physician performing the clinical investigation of joint inflammation was the same at each visit to avoid interpersonal variation in the assessment of articular disease activity. Two of the four JIA children showed some improvement of articular symptoms when put on a gluten-free diet. Conclusions, however, must be made with caution, because the overall effect of a gluten-free diet was not remarkable. All the children had systemic treatment for JIA and their articular symptoms and inflammatory markers were quite suppressed when they started the gluten-free diet. Because remission of the joint inflammation is associated with disappearance of gut inflammation in different forms of spondylarthropathies [18], it is likely that the degree of gut involvement was also low at the time of the study period. It can be speculated that the effect of the diet could have been more pronounced during an acute phase of arthritis.

Patient	1	2	3	4
Gender (M/F)	M	F	F	F
Age (years)	5	11	12	9
Duration of JIA	11 months	20 months	12 months	>3 years
HLA-B27	-	-	-	+
S-Ana-Ab	+	+	+	-
GI-symptoms after diet	↓↓↓	↓	↓↓	↔

Table 1: Clinical characteristics of the four children with juvenile idiopathic arthritis (JIA) exposed to gluten free diet for three months. Subjective symptoms after gluten free diet modification (↓↓↓ obvious relief, ↓↓ some relief, ↓ minor relief, ↔ no relief).

	Patient 1			Patient 2			Patient 3			Patient 4		
	screen	mixed diet	gluten free	screen	mixed diet	gluten free	screen	mixed diet	gluten free	screen	mixed diet	gluten free
VAS doctor	20	13	10	4	5	2	0	30	11	0	0	0
active joints	2	2	1	2	2	1	0	8	2	0	0	0
CHAQ	0	0,25	0,125	0,125	0	0	0,25	0,875	0,875	0,5	0,25	0,375
VAS patient	0	0	0	5	0	0	17	41	38	24	19	26
JADAS10	4	3,6	2	2,9	2,5	1,2	1,7	15,1	6,9	2,4	1,9	2,6
ESR	16	23	10	10	6	7	3	4	6	7	9	10

Table 2: VAS (Visual Analogue Score: doctor's VAS, patient's/parent's VAS), number of active joints, and CHAQ (Children's' Health Assessment Questionnaire), ESR (mm/h), JADAS10.

Patient	1. Screening		2. After mixed diet		3. After a gluten-free diet	
	Gliadin-IgG (EIU) (<8)	Milk-IgA (%) (<6)	Gliadin-IgG (EIU) (<8)	Milk-IgA (%) (<6)	Gliadin-IgG (EIU) (<8)	Milk-IgA (%) (<6)
1	8.8	6.5	n.d.	n.d.	4.9	5.5
2	>40	35	>40	32	>40	31
3	8.4	4	6.1	1.7	4.5	2.3
4	7.4	20	5.8	16	4.3	17

Table 3: Anti-gliadin IgG antibodies and milk IgA antibodies in sera at screening, after three months on a mixed diet (no food restrictions and wheat allowed) and after three months on a gluten-free diet (normal values are shown in parenthesis). Values on bold are above reference range.

In conclusion, our short-term evaluation of the introduction of a gluten-free diet in four children with JIA showed a modest improvement of articular symptoms in two children who did not have celiac disease and had no anti-gliadin antibodies prior to the gluten-free diet.

Dietary evaluations are potentially feasible and important since the families have a growing motivation to dietary modifications even without sufficient background data. These kinds of evaluations are often difficult to conduct and the effects may be challenging to interpret. There are also other possible diet modifications besides gluten-free diet, e.g. vegetarian diet or dietary supplements but such arrangements are likewise challenging to conduct. Regarding potential future studies, the patients should preferably have more active disease in the beginning of the study than the patients had in the present study. Was this the case, demonstration of possible improvement if any would be more feasible.

This pilot study showed some likely problems that may be faced during large-scale studies. High-quality planning, adequate screening, and thorough follow-up, and motivation of the families are some of these important issues.

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