Therapeutic and nutritional applications of amino acid-based elemental formulas in children with food allergies: a preliminary report

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Abstract

Introduction: Amino acid-based elemental formulas (AAFs) are used for the treatment and nutrition of children with food allergies who show no clinical improvement when fed with extensively hydrolyzed casein-whey protein formulas (eHF) or who develop allergic reaction to these formulas.

Aim: To assess the therapeutic efficacy of amino acid-based elemental formulas in children with severe multiple food allergy (MFA).

Material and methods: The study group consisted of 67 children aged 3 months to 5 years, with a severe clinical course of atopic dermatitis, gastrointestinal or multiple organ symptoms of food allergy. These children had been given eHF without therapeutic effects and developed an allergic response to these formulas. Patients were qualified for treatment of AAF based on an analysis of their diet, the clinical symptoms, individual and family history of allergy, asIgE specific for cow's milk proteins class 2 (> 0.7 kU/l). The efficacy of dietary treatment assessed during check-ups was based on a subjective and objective examination, assessment of anthropometric parameters (body mass, height, and SCORAD index score in children with atopic dermatitis). Therapeutic efficacy and tolerance of AAFs were evaluated based on a 4-point scale: from grade 1 – complete recovery to grade 4 – no improvement.

Results: A satisfactory improvement of the clinical state was observed in 60 patients (90%). The best therapeutic effect was in children with multiple organ manifestation of a disease or atopic dermatitis – improvement in 14 (93%) and 33 children (91%), respectively. Three patients (4.5%) did not tolerate the taste of the formula, 2 (3%) had adverse reactions associated with the skin and GI tract.

Conclusions: The AAF had excellent therapeutic and nutritional efficacy in children with severe food allergy. Symptoms of AAF intolerance were only reported occasionally.

Key words: amino acid-based elemental formula, allergy to extensively hydrolyzed casein-whey protein formula, multiple food allergy, children.

Introduction

Numerous clinical and epidemiological studies conducted worldwide and in Poland within the last 30 years have shown an increasing prevalence (up to 8%) of common and recurrent organic and/or systemic conditions resulting from food hypersensitivity in children and adolescents. This problem also affects the adult population, although to a lesser extent (3-4%), partly because children outgrow their allergies and partly because the underlying cause is rarely identified [1].

Food hypersensitivity occurs in individuals with a genetic predisposition to "atopic" or allergic reactions [2]. In these individuals, food products induce a qualitatively different response involving allergic symptoms, compared with healthy individuals. Among formula-fed or mix-fed infants, the most common cause of such symptoms is cow's milk protein allergy, whose estimated prevalence in this population is 4-8% [3, 4].

Cow's milk protein allergy may also develop in exclusively breastfed infants born in "high-risk families" with

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a family history of this allergy. This clinical problem affects approximately 0.5% of all breastfed infants. Trace amounts of food products containing cow's milk eaten by a nursing mother may be excreted in her breast milk as allergens, leading to an allergic response in the breastfed baby [5, 6].

A common triggering mechanism of food allergy is gastroenteritis, leading to the loss of immune and biological tolerance to the consumed foods. Loss of tolerance results from impaired integrity of the gastrointestinal mucosal barrier, as well as an increased penetration of food antigens into the body, followed by their presentation to immunocompetent cells.

Some formula-fed and breastfed infants with symptoms of cow's milk protein allergy also develop multiple food allergy (MFA). In MFA, the clinical response is evoked by consuming not only cow's milk but also egg white, cereal proteins, soy, meat, fruit, vegetables and other food products. Paradoxically, hypersensitivity to extensively hydrolyzed formulas (eHF) or partially hydrolyzed formulas (pHF) can also be observed in these patients [7]. When administered, these formulas do not accomplish their therapeutic and nutritional roles due to the allergic response evoked by the residual native protein they contain. This native protein or peptides and/or their hydrolysis products sensitize T-cells through their linear epitopes [8, 9].

According to the Gell and Coombs classification, hypersensitivity and allergic symptoms induced by food, or therapeutic and nutritional formulas suspected of evoking adverse reactions, develop as a result of 4 potential pathogenic mechanisms: type I (IgE-dependent), type II (IgE-independent, cytotoxic), type III (immune complex) and type IV (delayed, cell-mediated) hypersensitivity [10-12].

The first atopic pathological mechanism can be identified by means of tests for allergen-specific IgE (asIgE) antibodies to cow's milk proteins, including casein, α-lactoalbumin, and β-lactoglobulin. In IgE-independent allergic mechanisms, the cause of the underlying hypersensitivity can be determined by using the diagnostic food elimination/challenge test [13, 14].

Allergic reactions to cow's milk protein and multiple other food allergies – MFA constitute serious epidemiological and clinical problems in children and adolescents [15]. Treatment of the different manifestations of this allergy is based on temporary elimination of one or more "harmful" food products. In cow's milk protein allergy, the treatment additionally involves therapeutic and nutritional administration of extensively hydrolyzed casein/whey protein formula (eHF) [16].

Therapeutic administration of protein hydrolysate formula fails in approximately 1-10% of patients with cow's milk protein allergy or other type of food allergies. This is because of a hypersensitivity response to "residual native protein" contained in these formulas [17]. The alternative is administration of "elemental" formulas in which the hydrolyzed cow's milk protein fraction has been substituted with synthetic amino acids, i.e. amino-acid-based formula (AAF) [18, 19].

The increasing problem of allergy to eHF in pediatric or adolescent patients with concomitant allergy to cow's milk proteins or other foods is not merely a regional clinical and epidemiological problem, but it also has nationwide and worldwide implications [20-22].

In our clinical centre, we have assessed the relative efficacy of dietary treatment using elemental AAF EleCare (Abbott, US) in the youngest patients with severe manifestation of cow's milk protein allergy or multiple food allergies.

Aim

To retrospectively assess the therapeutic and nutritional efficacy of AAF given to children with severe food allergy in whom:

- no clinical improvement was achieved following prior administration of casein/whey protein hydrolysate, and/or further progression of allergic symptoms was observed, or
- immunoclinical hypersensitivity symptoms occurred when protein hydrolysate formula was given.

Material and methods

This analysis was based on hospital and outpatient documentation of 77 children (21 girls, 56 boys) with severe allergy to cow's milk and/or MFA, exhibited as hypersensitivity to other foodstuffs. Between 2005 and 2010, these children were hospitalized in the Department of Pediatrics, Gastroenterology and Allergology of the Children's Teaching Hospital in Bialystok and received specialist care at the Outpatient Food Allergy or Gastrology Clinic of that hospital.

The age of treated children ranged from 3 months to 5 years (average: 14.7 months; 95% CI: 11.2-18.1 months). Infants constituted the largest group (Table 1). Patients participating in the study were diagnosed as having severe food allergy according to the classification of Vandenplas *et al.*, with account being taken of the prevalence and characteristics of isolated and co-occurring symptoms.

Patients were divided into 3 groups:

- group 1: 36 patients (54%) with severe atopic dermatitis and SCORAD index > 50%,
- group 2: 16 patients (24%) with the following GI symptoms: gastroesophageal reflux disease, diarrhea, vomiting, lack of weight gain, and malnutrition,
- group 3: 15 patients (22%) with concomitant multiple organ symptoms: skin, GI tract, respiratory system.

Patients were qualified for treatment with AAFs on the basis of:

- history of allergy, including both individual and family history,
- current nutritional patterns and the lack of therapeutic effectiveness of replacing milk formula with protein hydrolysates,

Table 1. Distribution of ages in children with food allergy

Age [months]	Atopic dermatitis *N* = 36 (54%)	Gastrointestinal symptoms *N* = 16 (24%)	Multiple organ symptoms *N* = 15 (22%)	Total *N*	Total %
3-6	7	6	1	14	21
7-9	10	1	2	13	19
10-12	6	2	1	9	13
11-18	5	1	5	11	16
19-24	5	3	3	11	16
25-36	2	3	3	8	12
> 36	1	0	0	1	1
Total	36	16	15	67	100

- clinical skin symptoms e.g. atopic dermatitis was assessed with the SCORAD index and children with a score > 50% qualified for treatment,
- level of asIgE, i.e. IgE against selected fractions of cow's milk proteins.

The total concentration of immunoglobulin E (IgE) and allergen-specific IgE antibodies (asIgE) against casein, α-lactoalbumin, and β-lactoglobulin was determined by a fluoroimmunoenzymatic method (UniCAP). Values > 0.7 kU/l (class 2) were accepted as positive asIgE results.

The causative role of initially harmful food allergens in triggering and sustaining allergic symptoms in the infants participating in this study was demonstrated in an open food elimination trial and a food challenge test according to cow's milk and eHF.

Children who had been diagnosed as being allergic to cow's milk proteins or having a multiple food allergy were initially treated with casein hydrolysate or whey proteins of cow's milk. This dietary treatment lasted 3-12 months, depending on its therapeutic effects.

The effectiveness of this dietary treatment was assessed during check-ups every 3 months. This assessment was based on:

- subjective examination, an interview with the parents of the children being treated,
- objective examination by a pediatrician based on an assessment of anthropometric parameters such as body mass, height, and SCORAD index in children with atrophic dermatitis.

Efficacy of dietary treatment was assessed by IgE assays against fractions of casein or whey protein. After a period of individual observation, whenever it was found that treatment had not been effective, patients with a positive assay for these antibodies (greater than class 2) and/or a positive result of the challenge test with casein/whey hydrolysate were put on the elemental formula. Treatment lasted 3-12 months; responsive patients in whom it produced good effects and those who required further treatment continued to receive the elemental diet for more than 12 months.

The therapeutic effect of elemental AAF was assessed on the basis of a conventional 4-point scale. Improvement was considered complete (grade 1) when symptoms disappeared, making it possible to discontinue pharmacological treatment. In children with atopic dermatitis, a complete improvement means that the SCORAD index was reduced by 70-100%. Improvement was considered partial (grade 2) if a significant alleviation of symptoms was achieved and the SCORAD index was reduced by 30-70%, making it possible to limit pharmacotherapy.

Improvement was considered insignificant (grade 3) if only a slight alleviation of symptoms was achieved, necessitating further pharmacological treatment, and the SCORAD index was reduced by less than 30%. Grade 4 meant that no clinical improvement was achieved despite providing the elemental formula along with pharmacological treatment.

Results

Clinical symptoms

The majority of children (36; 54%) had the skin form of food allergy, i.e. atopic dermatitis. Sixteen children (24%) had GI symptoms, while 15 (22%) showed multiple-organ food allergy.

Immunological indices of the disease process

The IgE were found to exceed age-normal values in 27 children (75%) with atopic dermatitis, in 10 children (67%) with multiple-organ food allergy and in 3 children (18%) with GI symptoms. Values were highest in children treated for atopic dermatitis and ranged from 18 to 5,000 IU/ml (median 487 IU/ml); in 5 patients (14%) concentrations exceeded 5,000 IU/ml (Table 2).

Allergic reactions to cow's milk protein measured as the level of asIgE against the 3 main milk fractions (of at

Table 2. The results of immunologic examinations. Values are numbers (%)

Feature examined	Atopic dermatitis *N* = 36	Gastrointestinal symptoms *N* = 16	Multiple organ symptoms *N* = 15	Total
Hypersensitivity to fractions for cow's milk protein – asIgE	20 (56%)	2 (12.5%)	9 (60%)	31 (46%)
asIgE for 3 fractions cow's milk protein	12 (33%)	1 (6%)	3 (20%)	16 (24%)
asIgE casein	18 (50%)	2 (12.5%)	8 (53%)	28 (42%)
asIgE α-lactoalbumin	16 (44%)	1 (6%)	8 (53%)	25 (37%)
asIgE β-lactoglobulin	16 (44%)	2 (12.5%)	4 (27%)	22 (33%)
Range of serum IgE concentrations [IU/ml]	19-5000	2-1645	3-4218	

least class 2) were diagnosed in 31 subjects (46%), of whom 16 (24%) were found to be simultaneously allergic to all 3 fractions. The most common sensitizer was casein (42%), followed by α-lactoalbumin (37%) and β-lactoglobulin (33%); the total is more than 100% because some individuals were allergic to more than one component. Allergic reactions to these fractions were most frequent in patients with multiple-organ allergy (9 patients, 60%) and atopic dermatitis (20, 56%). The IgE percentages against milk fractions of class 4-6 according to the manufacturer's classification were found to be highest in patients with atopic dermatitis.

Multiple food allergy

In addition to being allergic to cow's milk, a number of patients were also found to be hypersensitive to other foods, mostly to egg white, wheat, gluten, pork, potatoes, carrots and fish. This was confirmed by the presence of asIgE in 25 patients (69%) with atopic dermatitis. In this group, 9 patients (25%) were confirmed to be allergic to 5 or more food allergens (Table 3). Additionally, 6 children (40%) from the group with multiple-organ symptoms and 2 (12.5%) with GI symptoms were confirmed to have allergic reactions after ingesting several types of foodstuffs.

Table 3. Number of children with multiple food allergies in the group with atopic dermatitis (*N* = 36)

Sensitized to:	*N* (%)
1 food (milk)	11 (31%)
2-3 foods (including milk)	12 (33%)
4-5 foods	4 (11%)
> 5 foods	9 (25%)

After 12 months on the elemental diet, 3 children with severe atopic dermatitis and polyvalent allergy (allergy to food allergens and inhalant allergens) were observed to have achieved a clinical improvement and an increase in the levels of total and asIgE, both in response to previous allergens and to new food allergens.

Duration of elemental amino-acid-based formula treatment

The duration of treatment with AAF varied, depending on observed effects and clinical improvement. In one-third of patients, the elemental diet was used for 3 months; in 75% it was used for 3 to 12 months. A total of 11 children (16%) were placed on this diet for more than 12 months (Table 4).

Treatment with the elemental diet was prolonged either due to deterioration of the clinical condition after reintroducing the hydrolysate (eHF) into the diet, or in response to a positive result of the food challenge test for this type of therapeutic and nutritional formula.

The treatment completion date was set after good tolerance to hydrolysates had been confirmed in an open challenge test. Subjects continued the elimination diet based on hydrolysates of whey proteins or casein.

Effects of treatment with elemental amino-acid-based formula

Sixty patients (90%) had a complete or partial clinical improvement when on the AAF diet. Symptoms subsided completely in 18 patients (27%).

Table 4. The duration of the elemental amino-acid diet (children – 67)

Duration of diet [months]	3	6	9	12	> 12
Total, *N* (%)	22 (33%)	14 (21%)	10 (15%)	10 (15%)	11 (16%)

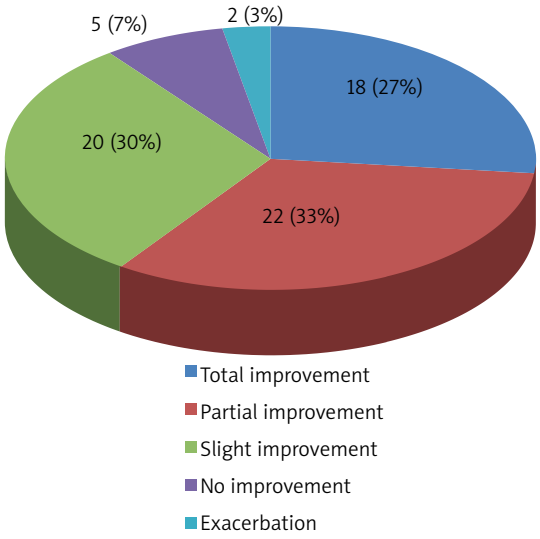

Fig. 1. Therapeutic effect of dietetic treatment in the study group

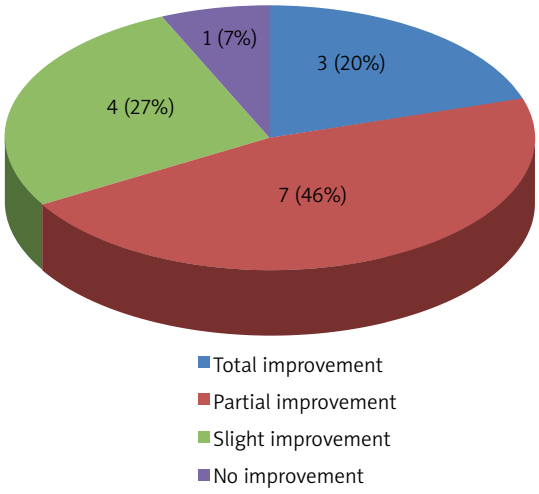

Fig. 2. Therapeutic effect of AAF diet in the group with multiple organ symptoms

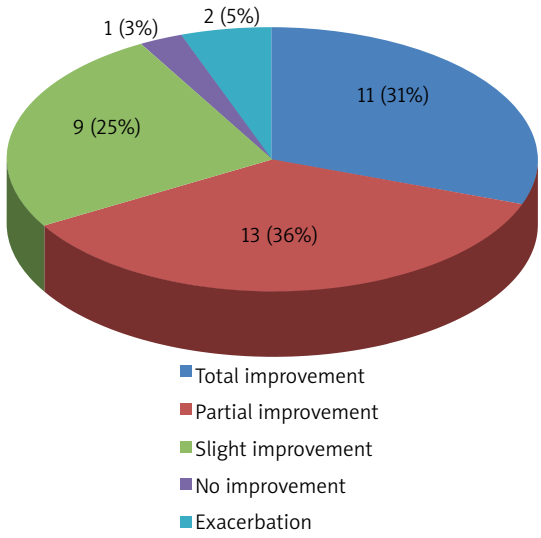

Fig. 3. Therapeutic effect of AAF diet in the group with atopic dermatitis

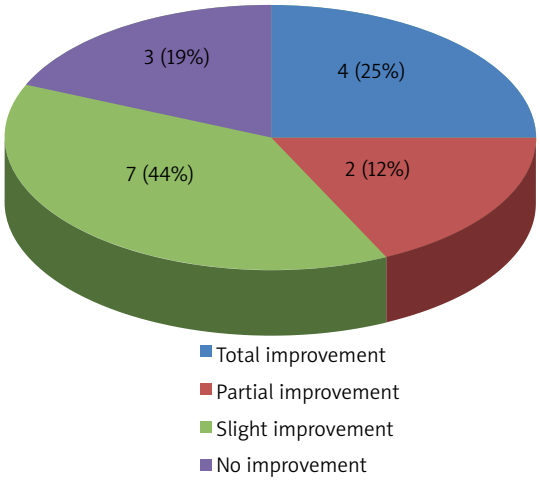

Fig. 4. Therapeutic effect of AAF diet in the group with gastrointestinal symptoms

Partial improvement was achieved in 22 children (33%) treated with the AAF; while in 5 patients (7%), the formula failed to produce any clinical improvement (Figure 1).

Effects of treatment on various forms of allergic disease

Treatment with elemental AAF was most successful in children with multiple-organ and skin-type food allergy; improvement was recorded in 14 patients (93%) and 33 patients (91%), respectively (Figures 2, 3).

A complete improvement, i.e. total disappearance of symptoms, was achieved in 11 patients (31%) with atopic dermatitis. In the group with multiple-organ allergies, a partial improvement was observed in nearly half the children (7 patients, 46%) receiving treatment (Figure 3).

A therapeutic effect was achieved in 81% of patients with persistent GI symptoms, in most of whom a slight improvement was recorded (Figure 4). The relative proportion of patients with IgE-dependent allergy to cow's milk proteins was found to be the lowest in this group.

Evaluation of the tolerability of the elemental amino-acid-based formula

Symptoms of intolerance to the elemental formula were observed among the treated children. Of these, 3 children (4%) could not tolerate the taste. Concomitant

adverse effects were observed in 2 patients (3%), specifically intensification of skin symptoms was seen in both patients, one of whom also had deterioration of stool consistency (1.5%) while the other exhibited anxiety (1.5%).

Treatment with EleCare formula was discontinued in these children and replaced with the Neocate elemental formula.

Discussion

The estimated prevalence of cow's milk protein allergy is 4-8% [3, 4] in formula-fed infants and 0.5-1% in breastfed infants [5]. In approximately 22-47% of the patients with cow's milk protein allergy treated with an elimination diet, tolerance to cow's milk protein develops with age. Nevertheless, these infants are prone to adverse reactions or hypersensitivity to other foods [7].

Hypersensitivity to hydrolysate formulas based on casein, whey or soy isolate constitutes a significant treatment difficulty in these patients [11, 21]. This problem of allergy to hydrolyzed protein formulas used to treat food allergies, whose estimated prevalence is 1-10%, was noticed and described over 12 years ago.

These initial reports by Businco *et al.* [8], Hill [20], de Boissieu *et al.* [17], Vanderhoof *et al.* [21], and in Poland by Kaczmarski *et al.* [23] indicated the clinical and therapeutic importance of this type of hypersensitivity. On one hand it affects the efficacy of the administered treatment, while on the other, it is often associated with MFA. The prevalence of multiple food hypersensitivity in children under the age of 3 is approximately 3-8%. This hypersensitivity is usually the main cause of the lack of improvement observed following administration of therapeutic and nutritional hydrolyzed protein formulas [15, 24].

According to the Position Statement of the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), the extensively hydrolyzed casein or whey-based formulas should be used in the treatment of cow's milk protein allergy [25]. Extensive protein hydrolysis causes a significant reduction in the antigenic properties of peptides and extensively hydrolyzed formulas (eHF) have reduced allergenic potential. However, they taste and smell much worse and the entire diet is more expensive.

Therefore, based on the experience of ESPGHAN Committee members, our own experiences and published data, it is recommended that patients with "severe food allergies" in whom treatment with extensively hydrolyzed protein formulas does not lead to satisfactory outcomes or who are hypersensitive to casein or the whey fraction of cow's milk protein should be treated with elemental AAF in their diet [25]. Since the protein fraction in AAF is substituted with synthetic L-amino acids, its allergenic properties are removed [26, 27].

General clinical indications for AAF include GI failure (impaired digestion, limited nutrient absorption area) and food allergy. Specific clinical indications for potential dietary treatment with elemental formula include: 1) severe manifestation of cow's milk protein allergy or multiple food hypersensitivity with concomitant allergy to therapeutic and nutritional formulas (fully hydrolyzed casein/whey fraction, or soy-based formulas) and/or other protein-based foods – multiple food allergy, 2) food-induced enteropathy, 3) multiple organ manifestation of food allergy with concomitant symptoms, e.g. severe atopic dermatitis, asthma, gastroesophageal reflux disease (GERD), 4) alarming symptoms of food allergy (malnutrition, hypoalbuminemia, anemia), 5) growth and weight gain disorders, 6) anaphylaxis.

The absolute indications for switching from therapeutic and nutritional formulas to elemental AAF are shock or shock-like reactions to hydrolyzed casein fraction or whey, as well as an allergy to soy and/or other protein-based foods [8].

One to ten percentage of children with cow's milk protein allergy show symptoms of hypersensitivity to extensively hydrolyzed formulas and approximately 30-50% of treated children are hypersensitive to soy-based formulas [21]. This phenomenon is mainly due to the technological process of protein hydrolysis and the residual content of native proteins in these formulas. The formula manufacturing process leading to exposure of new epitopes on the polypeptide chain may also have a significant impact. These epitopes, when presented to immunocompetent cells, may eventually lead to a sustained hypersensitivity reaction.

In patients with cow's milk protein allergy or MFA treated with hydrolyzed protein formula in whom allergic symptoms persist or increase, the titer of asIgE should be measured in response to casein, β-lactoglobulin and α-lactoalbumin [26-28]. If these tests are positive, elemental AAF should be given [29, 30]. In specific individual patients in whom this type of atopic allergy to the itemized protein fractions has not been confirmed by laboratory tests, this type of diet should be considered *ex juvantibus* after taking into account the IgE-independent hypersensitivity mechanism [28].

Not only is the protein fraction modified in elemental AAF, the carbohydrate fraction is composed of maltodextrins, corn syrup, glucose syrup and tapioca – all of which increase the osmolarity and caloric value of the formula. The fat fraction is composed of vegetable oils such as sunflower, soy and coconut oils. Additionally, it is enriched with medium chain triglycerides (MTCs).

The advantages and benefits of the elemental diet primarily involve immune effects, specifically reduced antigen exposure and synthesis of allergic inflammatory mediators. This therapy leads to the "sealing" of the gastrointestinal mucosa, which decreases the loss of proteins and micronutrients. As a result, protein balance is improved and any potential deficiency is compensated for. The efficacy of this elemental AAF diet in patients with

Table 5. Evaluation of efficacy of an elemental amino-acid diet according to the data from the literature

Author	Publication	Results of examinations
Hill *et al.* [11]	Allergy Clin Immunol 1995; 96: 386-94	In 18 infants with a delayed reaction to extensive hydrolysates – improvement after Neocate
Niggemann *et al.* [14]	Pediatr Allergy Immunol 2001; 12: 78-82	In infants with CMA with atopic dermatitis and no improvement after hydrolysates – improvement after Neocate
Sicherer *et al.* [27]	J Pediatr 2001; 138: 688-93	In 29 children with MFA and intolerance of hydrolysates – improvement after EleCare
Kanny *et al.* [32]	Allerg Immunol (Paris) 2002; 34: 82-4	In infants with MFA and no recovery after hydrolysates, improvement after AAF
Vanderhoof *et al.* [31]	JPGN 2008; 47: 60-1	According to 83% of parents, positive assessment of effect, treatment and tolerance of Nutramigen AA in children with allergy to milk

selected conditions has been assessed in several clinical centers for food allergy treatment (Table 5) [31, 32].

Our own study confirms the conclusions of the quoted authors. Among 67 children with different clinical manifestations of severe food allergies not responding to standard dietary treatment with eHF, the elemental formula-based diet led to improvement in 90% of patients. Taking into consideration the nature of this condition, the highest efficacy (93%) was in children with multiple organ manifestations of food allergy, although a partial improvement was reported more frequently (46%).

At the same time, the highest percentage of complete symptom resolution (31%) was reported in patients with atopic dermatitis. This result forms a good basis for further in-depth assessment of the efficacy of an elemental AAF diet administered to this group of patients as they are the most prone ones to develop MFA and subsequent dietary restrictions. The group of children with severe atopic dermatitis also displayed the highest percentage of patients with acute allergic responses and the highest total IgE titers [33]. The lowest efficacy of the elemental diet was in children with GI symptoms, although the overall improvement in this group was comparable to that achieved in other patients. In these patients, acute allergic responses played a minor role in the pathogenesis of the observed symptoms, which were primarily due to a delayed response. It is possible that these patients would have benefited had they continued on the elemental diet for longer.

The modified composition of AAFs impacts their potential for intolerance and the occurrence of adverse reactions. The most commonly reported symptoms described in the published papers are mainly skin-related and are associated with allergy to vegetable peptides that contaminate the formula. The peptide contamination of the lipid fraction as well as its modified composition (MCT, other vegetable oils including soy oil) may induce a similar immune response leading to the occurrence of allergic symptoms [29, 30]. Morisset described children with adverse reactions to the Neocate formula, who responded with symptom resolution within 2-4 weeks to a diet based on the Neocate Advance formula, which does not contain soy oil [31].

Reported adverse reactions to elemental formulas, occurring due to their increased osmolarity or maltodextrin intolerance include GI symptoms (osmotic diarrhea, flatulence and abdominal pain).

Our own observations involve AAF intolerance symptoms. Three children did not tolerate the taste; therefore the elemental diet was withdrawn from their diet. The taste of elemental AAF is a result of the manufacturing process which results in extensive protein hydrolysis. This response is also commonly observed in older children previously fed with other hydrolyzed casein or whey-protein formulae.

In 2 other patients, concomitant skin and GI adverse reactions occurred, which resolved following the introduction of another soy-free elemental AAF.

This study conducted in our center to assess the therapeutic efficacy of the elemental AAF diet used in patients with various manifestations of cow's milk protein allergy and MFA, is the first study of this type in Poland. The number of children who are likely to benefit from an elimination diet using AAF is still on the increase. This shows that the problem of severe food allergies and cow's milk protein allergy is increasing as well.

Therefore, the cessation of dietary treatment with hydrolyzed protein formulas must be considered as a distinct possibility. AAFs are available in Poland only by way of direct import, and the cost of such diets is quite high. The results of our study are encouraging and emphasize the need to monitor and maintain this type of treatment in children with severe food allergy caused by MFA. Good therapeutic outcomes achieved in children with severe atopic dermatitis encourage us to continue the elemental AAF-based diet for longer periods of time, until an age when they can potentially develop tolerance to the formerly harmful food allergens and new items can be safety introduced to their diet.

Conclusions

The elemental AAF was generally well tolerated; intolerance symptoms were observed only sporadically in the study population. In most patients with severe food allergy manifested by atopic dermatitis and multiple organ symptoms, elemental AAF provides excellent therapeutic outcomes.

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