Acta Derm Venereol (Stockh) 1992; Suppl. 176: 113–116

Extreme Dietary Measures in the Management of Atopic Dermatitis in Childhood

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Of 63 children with severe atopic dermatitis who were treated with a diet eliminating all but 6 foods for a 6-week period, 9 (14%) abandoned the diet, 21 (33%) completed the diet but did not benefit, and in 33 (52%) there was significant benefit. However, the outcome at 12 months was the same regardless of the response to the diet because of the tendency for dermatitis to markedly improve in all three groups. Of 37 children with exceptionally severe atopic dermatitis treated with an antigen avoidance regimen comprising hospitalization, exclusive feeding with an elemental formula for a median duration of 30 days, and measures to reduce exposure to pet animal and dust mite antigens at home, 10 (27%) either failed to respond to the regimen or relapsed within 12 months, and sustained improvement was seen in 27 (73%) patients. A few-food diet or a strict anti avoidance regimen may be associated with improvement of atopic eczema where conventional treatments have failed. ***Key words: atopic dermatitis; food allergy; diet.***

Acta Derm Venereol (Stockh) 1992; SUppl. 176: 113–116.

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Despite the most intensive application of conventional treatment (1), a small proportion of children with atopic dermatitis (AD) remain seriously handicapped with severe and widespread eczematous skin lesions. In such extreme cases, the traditional additional therapeutic options are unappealing. They comprise the application of potent topical steroids to large areas of skin, with the risk of skin atrophy and growth stunting, the use of systemic steroids, with the risk of growth stunting, cataract, osteonecrosis and other side effects, or doing nothing and leaving the child chronically handicapped and unable fully to engage in normal activities. Recent experimental approaches, such as photochemotherapy, cyclosporin, cytotoxic agents and interferon-γ are no more attractive (2).

Where a case of AD is refractory to conventional treatment, the question arises as to whether part or all of the disease can be attributed to allergic reactions to items such as food, pet animals or dust mites. Unfortunately, neither skin prick tests nor RAST tests can indicate which patient will respond to antigen avoidance, or which items should be eliminated (3, 4). The lack of predictive tests has led to the use of empirical diets in which a number of foods are avoided for a defined period of time (e.g. 6 weeks) (4). The failure of simple diets (e.g. egg and milk avoidance) has led to more rigorous forms of food elimination. We report on two fairly extreme antigen avoidance regimens, a few-food diet (5) and the use of a so-called elemental diet combined with measures to reduce exposure to pets and dust mites (6).

METHODS

Patient selection

Since 1980, 600 children with AD, who fulfilled the diagnostic criteria of Hanifin & Rajka (7), have been referred to the Department of Child Health at Booth Hall Childrens Hospital. Of these 600 patients, 63 were selected for few-food diet, either because of extensive (> 30% skin surface area) skin involvement poorly responsive to conventional therapy, or because of a clear history of food intolerance. Those with a history of food intolerance were already avoiding the foods concerned. In 43 patients, including some who had failed to respond to a few-food diet, the disease was very widespread, severely incapacitating, and unresponsive to conventional therapy, and the situation so desperate that the patient was considered for an extreme antigen avoidance regimen including an elemental diet in hospital using Vivonex (Tolerex) Standard (Norwich Eaton Pharmaceuticals Inc, 17 Eaton Avenue, P.O. Box 231, Norwich, NY 13815, USA). One family declined this approach, and 2 children aged 4 and 11 years refused to drink Vivonex, so the procedure was abandoned. Data on the 37/40 patients who had been followed up for 12 months or longer were analysed.

Patient assessment

The proportion of skin surface area affected by dermatitis (defined as patches of erythema, vesicles and crusts) and the degree of erythema (graded as mild = 1, moderate = 2, severe = 3) were recorded. The surface area and the erythema score were multiplied to give a combined disease severity score. Topical corticosteroids were classified according to the British National Formulary (8) as category IV (mildly potent) category III (moderately potent), category II (potent) or category I (very potent).

Few-food diet

The few-food diet consisted of six items: lamb, potato, rice, rice krispies, carrot and pear, and was given for 6 weeks. No other foods were permitted, and only water was allowed as a drink. Where there was a history of intolerance to or dislike of one of these six foods, then one of a small number of alternative foods was given instead (5). Twenty infants were given Pregestimil (Bristol-Myers Pharmaceuticals, Ickenham, Uxbridge UB10 8NS, England), a casein hydrolysate milk formula.

After 6 weeks the patient was reviewed. In the event of failure, defined as a less than 20% improvement in the disease severity score, the diet was discontinued. Those patients who were avoiding a small number of foods prior to the study continued to avoid these foods if the six-food diet was abandoned. If there was 20% or greater improvement in the disease severity score, then the diet was continued, and foods were reintroduced singly. Each new food was given daily for 7 days by open challenge at home, in quantities of 50–200 g, two to four times daily. The criteria for a positive challenge were 1) a sustained deterioration of dermatitis (increased scratching and visible worsening of eczematous skin lesions, lasting more than 24 h), or other adverse reaction (e.g. angi-edema or asthma) during exposure to the food; and 2) a return to the pre-challenge state after the food was withdrawn. If the second criterion was not met, the challenge was not classified as positive or negative, the food was avoided, and a repeat challenge was performed at a later date.

Table I. *Few-food diet: progress of disease severity, treatment and diet in patients who improved on diet.*

Time	Pre-diet	6 weeks	6 months	1 year
No. of patients	33	33	32	24
Disease severity score				
Median	70	20	10[b]	15
Range	20–240	4–180	0–140	0–180
Topical corticosteroid treatment				
None	6 (18%)	7 (21%)	7 (22%)	6 (25%)
Category IV	21 (64%)	23 (70%)	21 (66%)	13 (54%)
Category III+	5 (15%)	3 (9%)	4 (12%)	5 (21%)
Diet score[a]				
Median	2	7	6	5
Range	1–4	7	2–7	1–7

[a] *Diet score:*
1 Normal – no exclusions
2 Excludes 1 or 2 foods
3 Excludes 3 to 5 foods
4 Excludes 6 to 10 foods
5 Excludes > 10, includes > 20
6 Includes 10 to 19 foods
7 Includes < 10 foods

[b] Compared with the 6-week score, $p = 0.02$, (Wilcoxon matched pairs signed rank test).

Elemental diet

Removal of all mammalian and avian pets from the home was a prerequisite for treatment and was undertaken in 13 cases. The home was visited to ensure that rigorous measures (1) were taken to reduce house dust mite levels in the patient's bedroom. Corticosteroids were discontinued at the time of admission, but an emollient (emulsifying ointment) and night sedation (trimeprazine tartrate, 3 mg/kg (to a maximum of 60 mg) were continued. All patients were also given, because of the poor palatability of unflavoured Vivonex, cyproheptadine, an H1 receptor antagonist with some appetite stimulant effect (9), was also given until foods were reintroduced, in a dose of 2 mg twice daily. All normal food and drink (including water) were excluded, and the child was fed exclusively on unlimited quantities of unflavoured Vivonex. After 28 days of Vivonex given alone, if there was little or no improvement the diet was abandoned, and systemic or topical corticosteroids were used instead. If there was a moderate improvement the period of elemental diet was extended for another one to 2 weeks. If the dermatitis had largely resolved, then open food challenges were commenced. Foods to which the patient had a history of adverse reaction, and cow's milk, eggs, wheat, fish, nuts, tomato, citrus fruits and legumes were deliberately avoided for early challenges. In hospital, each new food was given in quantities of 50–200 g two to four times daily for a period of 7 days. During this time the patient's skin was observed 4-hourly for deterioration, and other indications of intolerance such as respiratory or gastrointestinal symptoms were noted. The criteria for a positive challenge were as above. Patients were discharged from hospital once established on three foods, at which point Vivonex was discontinued. Food challenges were continued at home and when positive the challenge was repeated at 6 to 12 monthly intervals. After discharge from hospital, the nutritional adequacy of the diet (10, 11) was monitored by means of 5-day diet surveys (12). If by 3 months after discharge the dietary intake of calcium was below the recommended daily amount (13), oral calcium supplements were given in the form of tablets containing calcium sodium lactate, calcium phosphate and vitamin D.

Table II. *Few-food diet: follow up results of all patients.*

		Pre-diet	6 weeks	6 months	1 year
Number attending follow-up					
Diet	Success	33	33	32	24
Diet	Failure	21	21	20	15
	N.C.	9	7	6	4
Median disease severity score					
Diet	Success	70	20	10	15
Diet	Failure	60	60	16	16
	N.C.	50	36	10	17
Proportion of patients receiving any topical steroid					
Diet	Success	82%	79%	78%	75%
Diet	Failure	95%	76%	90%	80%
	N.C.	100%	86%	100%	100%
Proportion of patients on category III or stronger topical steroid					
Diet	Success	15%	9%	12%	21%
Diet	Failure	24%	5%	20%	13%
	N.C.	33%	29%	50%	75%

N.C. = Patients who did not comply with diet.

RESULTS

Few-food diet

The median age of the patients was 2.9 years, 32 (51%) were girls, 46 (73%) had a history of food intolerance, 48 (76%) had previously tried other less stringent types of dietary restriction, and the median disease severity score at the start of the diet was 60. Nine patients (14%) abandoned the diet after a short period, but 53 (86%) completed the 6-week period of diet. In these there was a significant improvement in the disease severity score, from a pre-diet median of 60 (20–240) to 40 (4–270), $p < 0.001$ (Wilcoxon matched pairs signed rank test). Of the 54 patients who completed 6 weeks of diet, 21 (39%) showed little or no improvement, with a combined severity score of between 0.9 and 1.5 times the pre-diet score. There was no significant difference in age, pre-diet severity score, previous history of food intolerance, or previous dietary restrictions

Table III. *Elemental diet: Age of patients, pre-treatment disease severity, duration of hospitalization, strength of Vivonex and lowest serum albumin concentration.*

	Age (years)	Pre-treatment state of Eczema			Days in hospital	Days on Vivonex alone	Total days on Vivonex	Maintenance concentration of Vivonex (g/l)	Lowest serum albumin (g/100 ml)
		Surface area (%)	Erythema score[a] (%)	Combined score[b]					
Median	3.32	70	3	210	72	30	62	16.7	20
Range	0.45–13.23	20–96	2–3	60–288	45–189	7–43	7–124	13.3–26.7	9–32[c]

[a] 1 = Mild, 2 = Moderate, 3 = Severe.
[b] Combined score = surface area × Erythema score.
[c] Not recorded in 10 patients.

between the patients who did and did not respond to the diet. Six of the 21 diet failure patients, despite a lack of response to the diet, had adverse reactions to between one and four foods in the year following the trial of diet. Thirty-three patients (52% of those who started, and 61% of those who completed the 6-week period) showed a > 20% decrease in the disease severity score, and the subsequent progress of these patients is shown in Table I. On reintroduction of foods over the following year, 24/33 (73%) patients had adverse reactions to between one and eight foods (median 2.5), giving a total of 82 positive challenges. Forty-three out of 63 (68%) patients were followed up for 12 months or more. Regardless of the response to treatment, at one year the final outcome was very similar (Table II). For further details, see Devlin et al. (5).

Elemental diet

Details of the patients' age, pre-treatment severity of dermatitis, duration of the hospital admission, duration of use of Vivonex, maintenance concentration of Vivonex and lowest serum albumin are given in Table III. Four patients failed to respond to the regimen, and a further 6 responded initially but relapsed within 12 months. These 10 treatment failures were compared with the 27 in whom there was a sustained improvement, and no significant difference was found for age, sex, pre-treatment disease severity score, previous history of food intolerance, pre-treatment eosinophil count or serum concentration of IgE. With one exception, where clear improvement was seen within 7 days of commencing the elemental diet, the first signs of improvement were not seen for at least one, and more commonly 2 weeks. However it was usually only after 4 weeks of exclusive feeding on Vivonex that there was substantial improvement in the appearance of the skin lesions. The greatest improvement occurred during the period on Vivonex alone, when the median disease severity score fell to 27% of the pre-treatment score (range 3 to 67%). Before treatment, 14/27 (52%) had been using category IV topical corticosteroids, 12/27 (44%) had been using category III or II topical corticosteroids and 1 patient was receiving oral prednisolone. At the end of the Vivonex alone period, 26/27 (96%) were using emollients only, and the remaining patient was using a category III topical corticosteroid for small areas of dermatitis. By discharge from hospital, 24/27 (89%) patients remained on emollients alone, and 2 patients commenced category IV topical corticosteroids. Adverse effects of the regimen included weight loss and a fall in the serum albumin in most patients while on Vivonex alone, and loose stools (7 patients) while on Vivonex.

The detailed results of the food challenges are published elsewhere (6), but it was notable that of the positive food challenges in hospital, 5 were quick-onset reactions, with anaphylactic shock in 2 (14, 15), and 35 reactions were delayed in onset, and consisted of a deterioration in the patient's dermatitis, with a marked increase in itching and erythema. Seven of these reactions occurred between one and 24 h of starting the food, four began between 24 and 48 h after starting a food, and 24 (61% of all food reactions in hospital) were first noted only 2–7 days after introduction of the food. There was no correlation between the results of RAST testing and the outcome of food challenges.

Following discharge from hospital, a clear history of an allergic reaction to animals, house dust or grass was noted in 19/37 (51%) patients. For further details of results and a 6 year follow-up, see Devlin et al. (6).

DISCUSSION

The major drawback to these and other previous studies (16–21) of multiple food exclusion is the lack of a control group. This means that it is impossible to tell how much of the patients' improvement was due to a placebo effect. To perform a proper randomized controlled trial of this type of dietary therapy represents a major challenge, mainly because of the difficulty of devising a placebo diet, and in the case of elemental diets, the ethical difficulties of using a 2–3 month placebo period of hospitalization. The importance of controls could be no better emphasized than the results of the few food diet, where the outcome at one year was the same, regardless of the initial response to a diet, the overall improvement seen being a notable feature of the natural history of AD in childhood.

Delayed reactions to foods (22, 23) were a notable feature. There remains controversy about the existence of these reactions, and those who doubt their existence point to the lack of confirmation by double-blind placebo-controlled challenges. Again, the technical problems of achieving the 'blind' administration of normally consumed portions of food in carrier foods,

and given daily for 1 to 2 weeks, have not yet been surmounted, and it is likely that cast-iron proof of delayed reactions will be difficult to obtain in AD. Nevertheless, late reactions to inhalants are well known in asthma (24), and asthma has provided another model of late reaction, that of enhanced bronchial reactivity after food ingestion (25).

The role of these extreme dietary measures remains uncertain. The results of the few-food diet have made us less enthusiastic about this approach, but where the short-term gain which is associated with this diet is worthwhile, then it is a treatment which may be worth trying. Despite several limitations, the study of the elemental diet regimen, the only report of its kind, has demonstrated that a highly intrusive (minimum hospitalization 2 months) and potentially hazardous antigen avoidance regimen was associated with great benefit in some children previously handicapped by refractory widespread AD. This is clearly an approach to be considered as a last resort in exceptionally severe cases, bearing in mind that the major alternatives, of giving systemic steroids or doing nothing, are themselves associated with major drawbacks.

The potential hazards of diets (malnutrition and anaphylactic shock), and the need for very close monitoring, indicate that this is an approach that is best undertaken with full paediatric and dietetic support.

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