Antigen-free Diet in Adult Patients with Atopic Dermatitis

A Double-blind Controlled Study

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Munkvad M, Danielsen L, Høj L, Povlsen C O, Secher L, Svejgaard E, Bundgaard A, & Larsen P Ø. Antigen-free diet in adult patients with atopic dermatitis. A double-blind controlled study. Acta Derm Venereol (Stockh) 1984; 64: 524–528.

The efficacy of an antigen-free diet on the activity of atopic dermatitis was examined in a double-blind study, comprising 33 adults with severe atopic dermatitis. The antigen-free diet (Vivasorb®) was compared to a placebo diet during three weeks of hospitalization. Twenty-five patients were evaluable, two of whom had their diet stopped after a few days due to exacerbation. Nine patients improved, while 16 patients were unchanged. Among those who improved five patients had Vivasorb® and four placebo diet. In the remaining group 11 patients had Vivasorb® and five had placebo. Four patients reported of less pruritus, sleeplessness and antihistamine consumption (three Vivasorb,® one placebo) while 21 did not (13 Vivasorb,® eight placebo). Thus, there were no significant differences between the groups. Paraclinical studies of circulating eosinophilocytes, serum IgE, orosomucoid, HLA-antigens, and immunofluorescence of skin biopsies showed no differences between the Vivasorb® and the placebo groups. The results from the examination of this relatively small number of patients suggest that elementary intolerance plays little role in the etiology of atopic dermatitis in adults. *Key words: Alimentary intolerance; Adult; Antigen-free diet; Atopic dermatitis.* (Received April 19, 1984.)

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The predominant appearance of atopic dermatitis is a dry itchy skin developing eczematous areas following scratching. The itch seems to be provoked by several factors, i.e. physical irritants such as mechanical traumas, increased sweating, changes in humidity and other environmental factors, skin infections, phychological factors and allergic reactions. The present study is an attempt to evaluate possible aspects of food allergy. In the atopic disease complex several immunological manifestations, e.g. elevated IgE, increased number of circulating eosinophilocytes, and a high frequency of positive skin prick tests are common features. In allergic asthma and allergic rhinitis allergens are known to provoke the attacks (1). In atopic dermatitis, a similar etiology has been conjectured by many authors (2, 3, 4, 5, 6), but few double-blind and controlled studies support this concept (5, 6).

This study was inspired by the promising results in a similarly conducted trial by Høj et al. in patients with perennial asthma (7), and it was carried out in the same way to test whether an antigen-free diet given to adult patients with severe, atopic eczema during three weeks' of hospitalization was followed by any change in intensity or extension of the eczema when compared to a control group on placebo diet.

MATERIAL AND METHODS

Thirty-three adult patients with eczematous areas covering more than 10% of the body surface entered the study after informed consent. The criteria for diagnosis proposed by Hanifin & Rajka (8) were used.

Twenty-three patients, 15 women and 8 men, aged 16–52 years (mean 29 years) completed the trial without dietary lapses. Two women, aged 19 and 24 years, discontinued the diet after 3 and 4 days respectively because of severe exacerbation of the eczema. One patient was excluded due to Quincke's oedema and asthma on entering the trial, and one because of severe impetigo. Six patients withdrew for various reasons, mainly disliking the diet.

The 25 patients evaluated in the trial had periodically atopic dermatitis through 6 to 52 years (mean 27). When entering the study they presented eczematous areas covering from 25 to 91 % of the surface (mean 60 %). Eighteen of the patients had present or previous asthma, of whom 9 required treatment. Sixteen patients suffered from rhinitis, 2 had urticaria, 13 patients had a history of intolerance to one or more food elements, and 4 patients had gastrointestinal complaints.

When hospitalized the patients were randomized to a chemically defined antigen-free elemental diet regime or to a placebo diet, given orally during a period of 20 days. Vivasorb® without added taste (J. F. Phrimmer & Co., Erlangen, West Germany) containing essential fatty acids, amino acids, glucose, simple carbohydrates, vitamins, sorbic acid (15–40 mg/day) and trace elements (4000–10000 KJ/day) was used. Allowed supplements were mineral water and pure glucose. The placebo diet was composed of the foodstuffs and liquids consumed by in-patients of the hospital. It was blended and diluted with water to mimic Vivasorb®. Both were controlled by bacterial cultures and stored at −18°C until used. The diets were dispensed in opaque bags and drunk from opaque drinking cups, filled by the patients. To ascertain double-blindness patients and staff were told, that two different diets were given in order to test which one would be the best. The diets were delivered daily from the hospital kitchen by a dietary assistant, who never saw the patients.

In the pretesting phase 14 days before and during the trial the only treatment allowed was petrolatum with 5% carbamide, cyproheptadine, diazepam and paracetamol, when clinically indicated. Broncholytic treatment was continued in asthmatics.

Prior to and after hospitalization, two of us (M. M. and L. D.), who did not follow the patients in the ward, assessed the eczematous areas in percentage of the surface, and in the most badly affected areas, the degree of infiltration and hyperaemia (1+ to 3+). Whole body colour photos were taken before and after the diet period. A score between −3 and +3 was given to the degree of change for each of the clinical symptoms viz. erythema, infiltration and size of area involved. In addition a score was given to the degree of change visualized through pictures of the patients before and after

Table I. *Antigen-free diet to adult patients with severe atopic dermatitis during three weeks of hospitalizaiton*

A double-blind controlled study. Evaluation of changes in intensity and extension of the eczema ('major activity score')

	Vivasorb®	Placebo diet	Total
Improved	5	4	9
Unchanged	11	5	16

Table II. *Antigen-free diet to adult patients with severe atopic dermatitis during three weeks of hospitalizaiton*

A double-blind controlled study. Evaluation of changes in pruritus, sleeplessness and antihistamine consumption ('minor activity score')

	Vivasorb®	Placebo diet	Total
Improved	3	1	4
Unchanged	13	8	21

treatment. In the evaluation of the patients we used the mean value of these four figures multiplied with 100 named 'major activity score'. A major activity score exceeding 100 was the criteria for a positive response to treatment. Assessment forms about medicine intake and the patients' report on itching and nights' sleep were completed daily indicating 'minor activity score'. Wilcoxon Rank sum test for unpaired data was used in analysing the results. *Paraclinical studies* including counts of white-cells, platelets, and eosinophilocytes as well as orosomucoid were done every second day during the first and third week of the diet period. Serum IgG, IgA, IgM, IgE, α1-antitrypsin and bacterial culture from involved skin were assessed before and after the diet. Tissue typing with the HLA-ABC and the DR antigens was performed (9).

Two 3 mm punch biopsies were taken from normal and eczematous skin before and after hospitalization, one for usual histological examination, the other for immunofluorescence studies.

RESULTS

The 'major activity score' exceeded 100 in nine patients, i.e. the 'responder' group, viz. five on Vivasorb® and four on placebo. Sixteen patients did not benefit from the diet, i.e. 'non responders' viz. 11 on Vivasorb® and five on placebo (Table I). The 'minor activity score' showed improvement in four viz. three on Vivasorb®, one on Placebo, while 21 patients were unchanged or worse viz. 13 on Vivasorb®, eight on placebo (Table II). No significant differences between groups were demonstrated. A relationship between the clinical response to the different types of diet and a history of alimentary intolerance was not demonstrable (Table III).

The values of the Hb, WBC count, creatinine, orosomucoid, α1-antitrypsin, IgG, IgA and IgM were normal in all patients. The eosinophils showed significantly higher values in the two responder groups than in the two non-responder groups (Table IV). The serum IgE

Table III. *The patients' history of food intolerance before the trials as related to type of diet and clinical response*

	Vivasorb®	Placebo diet	Total
Improved	3	3	6
Unchanged	5	2	7

Table IV. *Serum eosinophils (mill/l) at the start (1) and the end (2) of the trial as related to type of diet and clinical response*

	Vivasorb®		Placebo diet	
	1	2	1	2
Improved	$n=5$		$n=4$	
Mean	1 119	955	2 099	1 419
Range	738–2 056	625–1 794	450–5 544	556–3 156
Unchanged	$n=9$		$n=5$	
Mean	354[a]	403	736	514
Range	163–994	50–656	425–1 356	369–725

[a] Mean value for all 11 non-responders given Vivasorb®, including the two patients having their diet interrupted, was 432.

was higher in the Vivasorb responder group than in the non-responder group given Vivasorb and vice versa in the groups on placebo diet (Table V). High values of IgE were related to treatment requiring asthma. There was no significant difference in eosinophils and IgE before and after the diet. The distribution of HLA-ABC and DR antigens in the patients with atopic dermatitis did not differ significantly from that of a control group. Furthermore, comparisons between the subgroups, i.e. responders versus non-responders to the antigen-free diet or the blended control diet did not show any significant differences.

Histological studies showed non-specific changes as seen in acute or subacute dermatitis, and in some patients the clinically uninvolved skin showed signs of chronic dermatitis. In immunofluorescence studies a wide variety of deposits were found in both normal and lesional skin of most patients, most often fibrin and C_3 in the corium and the vessel walls. The type and location of the deposits were not necessarily identical in eczematous and normal skin, and some had only deposits in the eczema. There was wide individual variation in the deposits, but no evidence of relationship between number, type of deposits or severity of the eczema. After the diet period changes in deposits were seen both in patients, who had had antigen-free diet, and in the control group. Generally, 'responders' (on both types of diet) had the same deposits before and after the diet period. In no case did they develop new deposits. Some of the 'nonresponders' who had Vivasorb® developed new deposits during the trial, some disappeared, and some remained unchanged.

DISCUSSION

The results obtained suggest that in adults alimentary intolerance play little role in the etiology of atopic dermatitis. The treatment period is rather short, but in our experience the disease activity may change radically over a few days. The higher values of serum IgE in the Vivasorb responder group as compared to the non-responder group given Vivasorb might support the prediction of Gleich & Muller (10) that patients with atopic dermatitis presenting elevated levels of IgE represent a group which benefits by allergen elimination. However, one would expect this responder group to be relatively larger than the placebo responder group. The anamnestic information of intolerance to food was not confirmed by the results, as there were both 'non-responders' and 'responders' on both types of diet. It

Table V. *Serum IgE (U/ml) at the start (1) and the end (2) of the trial as related to type of diet and clinical response*

	Vivasorb®		Placebo diet	
	1	2	1	2
Improved	n=5, 4 with asthma[b]		n=4, 0 with asthma[b]	
Mean	6 436	6 312	1389	1 605
Range	843–10 199	540–12 470	620–2 350	0–4 450
Unchanged	n=9, 0 with asthma[b]		n=5, 3 with asthma[b]	
Mean	1 651[+]	1 881	3 736	3 375
Range	40–4 515	39–5 934	380–11 884	435–8 402

[a] Mean value for all 11 non-responders given Vivasorb®, including the two patients having their diet interrupted, was 2 138. These two patients had asthma.
[b] Treatment requiring asthma.

is noteworthy that only 9 of the 23 patients improved, as a certain benefit from three weeks' hospitalization was expected.

The present study did not reveal any association between HLA antigens and atopic dermatitis or between HLA and responders or non-responders to the treatment. The immunofluorescence findings of fibrin and C_3 deposits in both normal and lesional skin are in accordance with earlier reports (11). The results suggest that deposits in normal and lesional skin of patients with atopic dermatitis are unrelated to severity or activity of the disease.

ACKNOWLEDGEMENTS

Tissue typing were carried out at the Tissue Typing Laboratory of the Blood Grouping Department, University Hospital (Rigshospitalet), Copenhagen. Vivasorb® was partly supplied by Phimmer A/S, Erlangen, West-Germany.

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