

## CLINICAL REPORT

# Sugar is Not an Aggravating Factor in Atopic Dermatitis

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**Patients with atopic dermatitis frequently blame food for worsening their eczema. Recently, a sugar-free diet has become very popular among German patients. In order to investigate whether sucrose is an aggravating factor in atopic dermatitis, we conducted a prospective study in 30 patients. Double-blind, placebo-controlled food challenges with sugar were performed during a sugar-free diet period, which was started one week prior to the first challenge. Study parameters included the SCORAD index and eosinophilic cationic protein levels, which were determined before diet, on food challenges and one day after. In 29 evaluable patients we observed no significant difference in study parameters after the verum challenge compared to the placebo challenge. From these results, we conclude that sugar is not an aggravating factor in atopic dermatitis, which contradicts the view of many patients and underlines the importance of evidence-based medicine in the guidance of patients. Key words: sucrose; adverse reactions to food; hypersensitivity reaction.**

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Adverse reactions to foods can aggravate the skin status in some patients with atopic dermatitis (AD). In childhood, allergic reactions are predominantly towards food items, whereas adults are more likely to have pollen-related food allergies (1, 2). Non-allergic, intolerance-like reactions can also trigger disease activity (3, 4). However, the perceived prevalence of adverse reactions to foods is more than 10 times higher than the true prevalence (5) and unsupervised diets are common among a large number of patients with AD (6, 7). In the UK, major dietary restrictions took place among 71% of children with AD, based on information received about the disease through the media or friends (6). In Norway 77/424 (18.2%) of patients with AD reported to have followed a diet, when asked about their experience with alternative medicine (7).

Recently, it has become very popular among German patients with AD to avoid sugar (sucrose). This is propagated by the media and even recommended by some doctors (8). Paradoxically, sucrose is often replaced by natural sweeteners such as honey or maple syrup, which contain glucose, fructose and, sometimes, even sucrose.

As yet, there are no controlled studies supporting a possible influence of sucrose on the skin status in patients with AD. We have therefore conducted a prospective study to investigate this issue by double-blind, placebo-controlled food challenges after a strict elimination diet.

## MATERIAL AND METHODS

### *Patients*

Thirty outpatients (24 females and 7 males including 9 children) were recruited for the study. All of the patients had AD according to the criteria of Hanifin & Rajka (9) and a mean age of 25 years, range 2 to 47 years. Measurements of total IgE ranged from 13 to 7.840 kU/l, mean 945 kU/l.

Patients with diabetes and phenylketonuria were excluded from the study. In all 30 patients, haemoglobin A1c (HbA1c), a marker for the concentration of blood glucose used in diabetic patients, ranged within normal limits.

The study was approved by the local ethics committee, and all patients and parents gave their written informed consent.

### *Study design*

As illustrated in Table I, patients had to adhere to the diet as explained below for a period of 10 to 14 days. One week of diet before the food challenges provided a sufficient length of sugar elimination prior to DBPCFC, which was performed in a randomized order. The SCORAD index (10) and eosinophilic cationic protein (ECP) levels were chosen as study parameters. Briefly, the SCORAD index is based on objective signs of eczema as well as the subjective items pruritus and loss of sleep. The maximum SCORAD index is 103 points. The same dermatologist documented the scores, blind, throughout the entire study. A difference of two SCORAD indices  $\leq 15$  points was defined as constant skin status, and a change  $> 15$  points as worsening or improvement, respectively. ECP correlates with clinical disease activity (11–14) and was chosen as an objective parameter.

Blood glucose was measured one hour after each food challenge, but the results were not disclosed to the patient or doctor.

Four patients were asked to stop treatment with antihistamines (2 patients) and topical corticosteroids (2 patients), which was not allowed during the study. Use of systemic corticosteroids was not permitted, either.

Patients were instructed to keep a diary and to document daily pruritus using a score from 0 to 3 for the entire study.

### *Diet*

All patients received detailed personal instructions by a nutritionist regarding their diet free of sugar, sweets and alternative sweeteners such as honey, maple syrup and fruits. The children were instructed along with their parents. Instead of only excluding sucrose, any kind of sugar had to be avoided, as sucrose and/or its monosaccharides glucose and fructose are present in most sweet foods. On request, aspartame (Synopharm, Hamburg, Germany) was offered as a replacement for sucrose. Aspartame was chosen as the placebo for the following reasons: (a) there are no reports of a negative influence of aspartame on skin status in AD (15), (b) reports of adverse reactions to aspartame such as urticaria and angio-oedema have not been substantiated in double-blind, placebo-controlled studies of aspartame (15, 16), (c) aspartame has been used as a placebo for sucrose in studies investigating a possible effect of sucrose on behaviour and cognitive function (17), and (d) aspartame has no long-lasting taste.

### *Oral provocation tests*

On the day of the verum challenge, patients were exposed to 100 g sucrose, which by far exceeds the normal daily intake (17, 18). Children below the age of 6 years were given 40 g. The placebo challenge was

Table I. Study design. Sugar-free diet (see Methods) was given for the whole period (0–10 days)

	Day 0	Day 7	Day 8	Day 9 or later	Day 10 or later
Study parameters	SCORAD	SCORAD, ECP, B-glucose	SCORAD, ECP <sup>a</sup>	SCORAD, ECP <sup>b</sup> , B-glucose	SCORAD, ECP <sup>a</sup>
Double-blind		Food challenge I		Food challenge II	
food challenges <sup>c</sup>					

<sup>a</sup>After the food challenge, eosinophilic cationic protein (ECP) was only determined if there was an aggravation of skin status.

<sup>b</sup>In children with a constant skin status, ECP was not determined on food challenge II.

<sup>c</sup>Placebo and verum were given in a randomized order.

given with 500 mg aspartame. Furthermore, 200 mg aspartame was added to both the placebo and verum, to ensure identical taste. Adult patients received their challenge in ice-cold black tea, and children in a dessert made of milk and starch. One gram of carob bean gum was added to the placebo tea drink to amend the viscosity.

#### Laboratory tests

Serum ECP levels were determined by an ELISA system (Pharmacia, Uppsala, Sweden) according to the manufacturer's guidelines. The cut-off level of the ELISA was 2 µg/l.

#### Statistical analysis

The Wilcoxon signed rank test for paired data was used for assessing skin status and ECP levels before and after one week of diet as well as after the challenges.

## RESULTS

Twenty-nine out of 30 patients were evaluable. In all 29 patients skin status and ECP levels remained constant during the entire study period. Minor changes after the sucrose (verum) challenge did not differ significantly from the changes after the placebo challenge. One patient was eliminated from the study because of violation of the study protocol.

#### Skin status

During the first week of sugar-free diet prior to the food challenge, no significant change in skin status was seen in the study population. The mean SCORAD index was 29.4 at the beginning of the study and decreased by 0.4 points after one week of sugar-free diet. There was no difference between children and adults (Table II). Twenty-four hours after the verum and placebo challenges, no significant change in skin status was seen (Fig. 1). There was an increase in the SCORAD index of 1.9 points after the verum challenge and a decrease of 1.2 points after the placebo challenge.

The difference in mean SCORAD points after the verum and placebo challenges was more pronounced in children than in adults, but did not reach statistical significance (Table II).

Table II. Change of skin status during the study, documented by mean SCORAD-points (and range)

	Before diet	After diet	After sucrose challenge	After placebo challenge
Whole group (n = 29)	29.4 (8–65)	29.0 (7–61)	+1.9 (–16 to 15)	–1.2 (–22 to 9)
Adults (n = 20)	28.3 (8–51)	28.9 (7–61)	+1.4 (–6 to 14)	+0.2 (–12 to 9)
Children (n = 9)	31.7 (13–65)	29.4 (8–60)	+3.1 (–9 to 15)	–4.4 (–22 to 2)

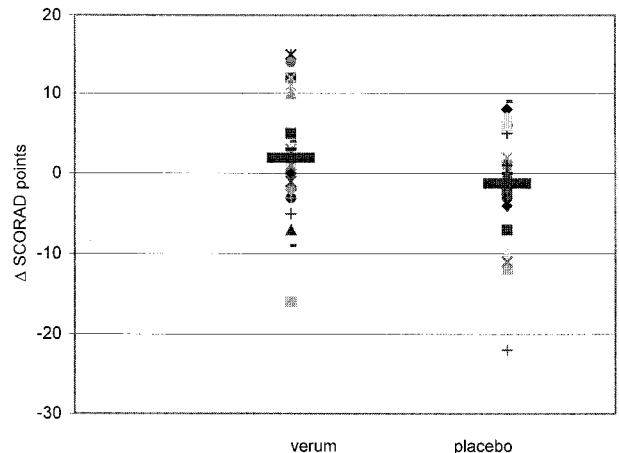


Fig. 1. Change in skin status in the study population ( $n = 29$ ) after the verum and placebo challenges, respectively, documented as difference in SCORAD points before and 24 h after provocation. The horizontal black bars depict the mean differences for both of the challenges. The difference in SCORAD points after the verum challenge did not differ significantly from that after the placebo challenge.

#### Laboratory parameters

The ECP levels ranged from  $< 2$  to  $74 \mu\text{g/l}$  with a mean of  $15 \mu\text{g/l}$ . No major changes in these levels were noted throughout the study (results not shown).

The rise in blood glucose after oral provocation was within normal limits. As expected, it was higher after verum than after the placebo challenge, although in most patients, there were only minor variations (results not shown).

#### Pruritus by patient diary

The patients' mean pruritus scores were not affected by either the verum or placebo challenge (pre-placebo: 1.05, post-placebo: 1.05 and pre-verum: 1.17, post-verum 1.22).

## DISCUSSION

In our study we were able to demonstrate that challenges with high amounts of sucrose, exceeding the normal intake, do not significantly affect the skin status or ECP levels in AD patients who have been on a sugar-free diet for one week. The SCORAD index increased after a sucrose (verum) challenge by 10 to 15 points in 7 patients, whereas no worsening was seen after a placebo challenge among the same patients. The intensity of aggravation in these 7 patients was within the constant range ( $\pm 15$  SCORAD points) and below the level regarded as a significant change in other studies (2, 19, 20). Thus, for challenges with food allergens, an increase in SCORAD above 30 points was requested (19, 20), whereas for pollen-associated food allergies, a rise in the SCORAD index above 15 points was regarded as positive (2). Only 2 patients had exacerbation of more than 15 SCORAD points when put on the sugar-free diet prior to DBPCFCs, probably because of stopping topical treatment on inclusion. Neither patient showed any difference in skin status after the verum or placebo challenge.

The possibility that the stability of skin status could be due to the withdrawal of sugar is contradicted by the outcome of the challenges. Among the 7 patients with an increase in SCORAD index of 10 to 15 points after the sugar challenge, only one patient had a pronounced reduction in SCORAD during diet. The remaining 6 had changes of SCORAD ranging between  $-4$  to  $+7$ . Although children had more pronounced changes in SCORAD than adults, they were all within the constant range, with the exception of one child, who had a decrease of 22 points after the placebo challenge.

Many patients with suspected food sensitivity "identify" the eliciting agent by self-administered exclusion diets (6, 21). However, the identification of possible eliciting factors is extremely difficult in a fluctuating disease such as AD. The results of the present study underline the general demand to critically evaluate the clinical relevance of suspected food items in each patient by double-blind placebo-controlled challenge before recommending dietary restrictions. Although eliminating sucrose from a diet will not cause deficiencies, every diet of uncertain benefit should be avoided. Childhood dietary restrictions in particular can readily add additional psychological stress, which is known to be a triggering factor in itself (22).

In conclusion, we have demonstrated that sugar is not an aggravating factor in AD, contrary to the view of many AD patients. Sugar should not be avoided by AD patients.

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