

## ORIGINAL ARTICLE

# A Popular myth – low-histamine diet improves chronic spontaneous urticaria – fact or fiction?

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## Abstract

**Background** Chronic spontaneous urticaria (CsU) is a frequent dermatological disease that might last for months or years with high impact on quality of life. Known causes are autoreactive phenomena, infections or intolerances, rarely IgE-mediated allergies. One-third of CsU patients benefit from a low-pseudoallergen diet. Additionally, it is often discussed, that reducing histamine ingestion alone might improve clinical symptoms and quality of life in CsU patients despite the uncertain role of the histamine-degrading enzyme diamine oxidase (DAO).

**Objective** Aim of this study was to investigate the impact of low-histamine diet on symptoms and quality of life in patients with CsU.

**Methods** Patients suffering from CsU accompanied by gastrointestinal symptoms were included in the study. They underwent low-histamine diet for at least 3 weeks. During the whole study, urticaria activity score (UAS) was recorded daily in a patient's diary. Quality of life was assessed during screening, baseline and post diet visits by completing questionnaires (DLQI and Cu-Q(2)oL). DAO activity was measured before and after elimination diet.

**Results** A total of 75% of the patients had a benefit from the low-histamine diet. Thirty-four of 56 patients (61%) reached the primary endpoint of the study, an improvement of UAS 4 of  $\geq 3$ . Overall, a significant reduction from 9.05 to 4.23 points ( $P = 0.004$ ) was achieved; the average reduction in a strongly affected subgroup was 8.59 points ( $P < 0.001$ ). DAO activity remained stable.

**Conclusion** Low-histamine diet is a therapeutically useful, simple and cost-free tool to decrease symptoms and increase quality of life in CsU patients with gastrointestinal involvement. Further research is needed to understand the role of diamine oxidase.

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## Conflicts of interest

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intolerance is not fully understood. Previous studies demonstrated abnormalities in histamine metabolism in patients with chronic urticaria. Intraduodenal histamine application provoked an attack in 64% of patients.<sup>13</sup> Many patients with CsU complain of worsening of symptoms by consuming histamine-rich food, like red wine or matured cheese, but to the best of our knowledge, until now no studies are available supporting these observations.

Due to these facts, we hypothesized that a low-histamine diet might improve symptoms and quality of life in patients with CsU comparable to a low-pseudoallergen diet.

In cooperation with a nutritionist, people were asked to run a low-histamine diet over at least 3 weeks (Table 1). The survey was conducted by assessing the urticaria activity score (UAS), calculated by combining pruritus intensity and the number of daily weals in a score system.<sup>14</sup> In addition, quality of life questionnaires were obtained: using the Dermatological life quality instrument questionnaire (DLQI)<sup>15,16</sup> established for dermatological diseases and the chronic urticaria quality of life questionnaire (CU-Q(2)oL), an urticaria-specific quality of life questionnaire.<sup>17</sup> Diamine oxidase (DAO), the enzyme disintegrating histamine, was measured before and after dieting.

## Methods

### Subjects

In two specialized urticaria centres in Germany (Darmstadt, Mainz), patients suffering from CsU for at least 3 months (average: 25 months), accompanied by gastrointestinal disturbances (e.g. meteorism or diarrhoea) were enrolled in the study. Patients with a medical history of other causes of gastrointestinal

symptoms (i.e. lactose, fructose, sorbitol or gluten intolerance, sorbitol malabsorption, already diagnosed histamine intolerance, IgE-mediated food allergy, Crohn's disease, colitis ulcerosa, infectious diarrhoea etc.) were excluded. At screening (day-7 before starting the diet), 66 patients were enrolled. Starting with the screening day, patients continued their normal diet for another 7 days completing additionally a diary. After 1 week, 57 patients (excluding drop-outs and lost of follow-ups) underwent at least 3 weeks of low-histamine diet. In one patient, calculation of UAS4 score was not possible. Finally, 56 patients (42 women, 14 men) completed the whole study and were statistically analysed. UAS was recorded daily from screening to after-diet visit. Additionally, quality of life was examined by questionnaires. DLQI and CU-Q(2)oL were determined at screening, baseline and after dieting. DAO activity was measured by REA (radio extraction assay, manufacturer: Sciotec DAO-REA<sup>®</sup>, Tulln, Austria) in blood samples at baseline and after dieting. Patients were asked to take antihistamines only when needed. All antihistamines were allowed (cetirizine, levocetirizine, loratadine, desloratadine, rupatadine, fexofenadine, mizolastine, dimetinden), even an up dosing. No histamine liberating drugs were allowed.

Primary endpoint of the study was an improvement of the 4-day UAS4 of at least three score points during the last 4 days of the diet compared to baseline UAS4 (during the 4 days before starting the diet). Secondary endpoints were changes in quality of life by surveying the DLQI and the CU-Q(2)oL. Comedication and changes in headache or gastrointestinal discomfort as well as adverse events were recorded.

This study was conducted according to the Declaration of Helsinki and all patients provided written informed consent. Ethic approval from the two county ethics committees was obtained. For statistical analysis and figures, SPSS 20.0 was used.

**Table 1** Recommended food in histamine-reduced diet

<b>Dairy products:</b> milk, cream and sour cream, butter milk, cream cheese, soured milk, curd cheese	<b>Meat and eggs:</b> eggs, cooked ham, not cured beef, veal, pork, lamb, chicken
<b>Fish (fresh or fresh frozen):</b> plaice, coalfish, codfish, haddock, trout, hake, perch	<b>Spread:</b> butter, margarine, honey, homemade jam (permitted fruit only)
<b>Sweets and Goodies:</b> fruit drops, fruit gums, chewing gum, popcorn	<b>Desserts:</b> cold sweet soup, rice pudding, stewed fruit*, sorbet and ice cream, fruit yoghurt or curd cheese with fruit*, vanilla custard *(permitted fruit only)
<b>Fruits:</b> everything, except for strawberries, raspberries, citrus fruit, bananas, kiwis, plums, papaya	<b>Vegetable:</b> Any fresh or frozen vegetable, except for tomatoes, spinach, avocados, egg plant
<b>Cereals/Potatoes/Noodles:</b> bread and pastries, pasta, all kind of potatoes, cereals, grains (rice, corn, millet seed, buckwheat)	<b>Beverages:</b> Soda water, homemade fruit and vegetable juices*  *(permitted fruit only)

### Diet and medication regimen

All patients received a list of allowed food, composed by a nutritionist in accordance to the recommendations for histamine intolerance of the German Society of Allergy and Clinical Immunology (Table 1) and a diary for documentation of their daily ingested food and symptoms. No dietary supplements such as vitamins, homoeopathic substances, plant preparations, minerals etc. were allowed. Corticosteroids or medications for acute infection etc. were only approved if necessary and had to be documented. During the whole study, the patients were asked to take antihistamines only if necessary.

### Outcome measures

**Disease activity** The urticaria activity score was assessed daily. UAS4 scores were calculated by summarizing the scores 4 days before starting the diet and during the last 4 days before the end of the diet. UAS refers to the main symptoms: severity of itching and quantity of weals, including number of weals (0 = no