REPORT
RAPPORT

Benefits of a Histamine-Reducing Diet

for Some Patients with Chronic Urticaria and Angioedema

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Abstract/Résumé

Urticaria and angioedema symptoms result primarily from the physiological actions of histamine. Some individuals with urticaria have a decreased ability to degrade dietary histamine before it enters the circulation. Foods high in histamine, such as fermented foods, may exacerbate urticaria and angioedema in these individuals. Certain food additives may increase endogenous release of histamine and urticaria and angioedema symptoms. The objective of this study was to evaluate the effect of a histamine-reducing diet on urticaria and angioedema symptoms, and on nutrient intake. Nineteen subjects with chronic urticaria or angioedema were randomized to a treatment group (n=9) or a control group (n=10). The treatment group followed a histamine-reducing diet, and the control group eliminated artificial sweeteners from their diets. The subjects recorded antihistamine medication intake, number of wheals, the severity of pruritus and the severity of angioedema for two weeks before starting the diet and for six weeks during the dietary intervention. Subjects completed three-day food records every two weeks. There was a marginally significant decrease in the number of antihistamine tablets taken in the histamine-reducing diet group compared with the control group, and two of nine treatment subjects had dramatically improved symptoms. During the study there was no significant risk of nutritional deficiency for either group. (Can J Diet Prac Res 2000; 61:24-26)

Les symptômes de l'urticaire et de l'œdème angioneurotique sont causés surtout par l'action physiologique de l'histamine. Certaines personnes atteintes d'urticaire présentent une capacité moindre à dégrader l'histamine alimentaire avant qu'elle n'entre dans la circulation sanguine. Les aliments riches en histamine, tels les aliments fermentés, peuvent aggraver l'urticaire et l'œdème angioneurotique chez ces personnes. Certains additifs alimentaires peuvent accroître la libération endogène de l'histamine et, par ricochet, les symptômes de ces deux affections. L'objectif de l'étude était d'évaluer l'effet d'une alimentation à faible teneur en histamine sur les symptômes d'urticaire et d'œdème angioneurotique et sur l'apport en nutriments. Dix-neufs sujets souffrant d'urticaire chronique ou d'œdème angioneurotique ont été répartis au hasard en un groupe de traitement (n=9) et un groupe témoin (n=10). Les sujets du groupe traité suivaient un régime à faible teneur en histamine et ceux du groupe témoin éliminaient les édulcorants artificiels de leur alimentation. Les sujets notaient leur apport en médicaments antihistaminiques, le nombre de papules œdémateuses, la gravité du prurit et de l'œdème angioneurotique pendant deux semaines avant le début de l'expérience et pendant les six semaines de l'intervention alimentaire. Ils remplissaient des relevés alimentaires de trois jours toutes les deux semaines. On a noté une diminution significative marginale dans le nombre de comprimés d'antihistaminiques pris dans le groupe consommant une alimentation à faible teneur en histamine comparativement au groupe témoin et deux des neuf sujets traités ont vu leurs symptômes diminuer considérablement. Au cours de l'étude, il n'y avait aucun risque important de carence nutritionnelle dans les deux groupes. (Rev can prat rech diétét 2000; 61:24-26)

INTRODUCTION

Plasma histamine, an important mediator of urticaria (hives) and angioedema, may be increased by diet through two mechanisms. First, under normal conditions, dietary histamine is degraded in the intestine by mucosal diamine oxidase enzyme (DAO); this prevents histamine's entry into the circulation. However, in chronic urticaria, DAO activity is decreased (1) and dietary histamine may increase plasma histamine (2). Second, certain foods and food additives may increase the endogenous release of histamine (3,4); this results in increased plasma histamine. No research studies have evaluated the effect on symptom severity when these dietary factors are modified. The objective of this study was to evaluate the effect of a histamine-reducing diet on symptoms of urticaria and angioedema, and on nutrient intake.

METHODS

Individuals with urticaria and/or angioedema of over six weeks' duration and with ≥ one episode a week were recruited through newspaper advertisements. Subjects were excluded

Table 1
Histamine-reducing diet[1]

Eliminate foods with elevated histamine content:		
spinach	yoghurt	tomato products
sour cream	fish	processed meat
leftover meat	alcohol	fermented soy products
fermented foods		
Eliminate foods with histamine-releasing properties:		
strawberries	pineapple	tomato products
seafood	uncooked egg white	chocolate
Eliminate food products containing the following additives:		
benzoic acid	sodium benzoate	benzoyl peroxide
butylated hydroxyanisole	butylated hydroxytoluene	artificial food color
Eliminate foods high in natural benzoate:		
cranberries	strawberries	raspberries
prunes	cinnamon	anise
cloves	nutmeg	
Eliminate foods with >5 mg salicylate per common portion size:		
pineapple	dates	currants
raisins	prunes	curry powder
hot paprika		
Follow hygienic procedures for food storage and preparation.		

[1]Adapted from refs. 4, 6-8.

if they were ≥18 years of age; were changing medications to control symptoms; were pregnant, or had an infectious disease, urticarial vasculitis, mastocytosis, rheumatoid arthritis, or lupus erythematosus. The University of British Columbia Clinical Screening Committee for Research and Other Studies involving Human Subjects approved the study, and all subjects provided informed consent.

Subjects were randomized to a treatment or control diet and were followed for six weeks in a single-blind study. Subjects evaluated their symptoms each day for two weeks before initiating the diet (time 1) and for six weeks while following the diet (times 2, 3 and 4; two weeks for each time period). During each time period, subjects attended a follow-up appointment so that compliance could be monitored and instructions reinforced.

The treatment group was instructed to eliminate foods potentially high in histamine, and food additives or foods that may increase endogenous histamine release (Table 1). The control diet eliminated Aspartame™, Splenda™, Sunett™, saccharin, cyclamate, mannitol, xylitol, and sorbitol. Control subjects received diet instruction and follow-up appointments similar to those of the treatment group. Subjects were instructed to keep other factors that may affect symptoms consistent throughout the study, and to record any changes in these factors.

Each day, subjects recorded the number of antihistamine tablets taken, the number of wheals, and the severity of pruritus and angioedema (scale of 0 to 3, where 0=symptoms absent; 1=symptoms present, but barely noticeable; 2=symptoms definitely noticeable, but tolerable; 3=symptoms definitely noticeable, and not tolerable). During each time period, subjects also provided three-day diet records, which were analyzed with PC Nutricom V 5.03 (Delta Nutrition Systems; Vancouver, BC, 1994). A mean intake (70 % of the 1990 Canadian Recommended Nutrient Intakes (RNIs) (5) was considered a significant risk for deficiency. For each nutrient and group, a weighted RNI was calculated, based on the number of male and female subjects in each group.

The SPSS for Windows Version 6.0 (SPSS Inc.; Chicago, IL, 1993) was used for statistical analysis. Age, gender distribution, and disease duration were compared between groups with an independent samples t-test, a Mann-Whitney U test, and a Wilcoxon's signed rank test, respectively. Nutrient and symptom data were analyzed with 2 x 2 (group x time) RM ANOVA (with repetition on the time factor). Time 1 values for variables were compared with independent samples t-tests to identify significant baseline differences between groups. When present, a 2 x 2 (group x time) RM ANOVA (with repetition on the time factor) was conducted using time 1 value as the covariate.

RESULTS

One subject withdrew from the study, leaving ten subjects in the control group and nine in the treatment group. There were no significant differences in disease duration, age, or gender distribution between groups. At baseline, the treatment group took significantly more antihistamine tablets than did the control group (Table 2). The treatment group took fewer antihistamine tablets in time 2 than in time 1 ($p<0.05$), and there was a marginally significant decrease in antihistamine tablet use over the four time periods in the treatment group versus the control group (Table 2). There were no significant differences between groups for number of wheals or for severity of pruritus or angioedema.

Immediate and near-complete symptom remission occurred in two of nine treatment subjects (responders). Two other subjects had partial remission.

One responder had an eight-month history of urticaria and angioedema.

Table 2
Number of antihistamine tablets (mean ± SD) taken two weeks before (at baseline) and six weeks during implementation of a histamine-reducing or control diet

GROUP	Time 1 (baseline)	Time 2	Time 3	Time 4
Treatment (n=9)	17.5 ± 11.5*	11.5 ± 13.0**	11.0 ± 13.0	11.5 ± 14.0***
Control (n=10)	7.5 ± 6.5	7.5 ± 5.0	7.0 ± 6.0	7.5 ± 4.5

* $p<0.05$ treatment versus control at baseline

** $p<0.05$ (time 1 vs time 2); no significant difference in the control group

*** marginally significant decrease over time (significant group x time interaction $F=3.46$, calculated $F=3.15$; $p<0.05$)

Major symptoms disappeared on day 1 of the study. During the two weeks before the treatment diet, this subject took 13 antihistamine tablets, compared with two tablets during the six weeks on the diet. The subject also discontinued use of a topical corticosteroid.

The second responder had a 20-year history of urticaria and angioedema. Symptoms disappeared and antihistamine medication was discontinued on day 4 of the treatment diet.

Five months after completing the study, both subjects were following the histamine-reducing diet. Their symptoms were controlled.

Group mean nutrient intakes were >70% of RNIs at all times. However, significant group-by-time interactions were detected for calcium, total fat, and vitamin C. Calcium and fat intakes were lower during the intervention in the treatment group and did not change in controls, but intakes at time 4 were similar (644±174 vs 680±325 mg calcium and 63±18 vs 62±33 g fat for treatment and control groups, respectively). Vitamin C intake increased in the treatment group and did not change in controls, with time 4 intakes of 170±94 vs 90±69 mg, respectively.

DISCUSSION

Adherence to the histamine-reducing diet for two weeks significantly reduced antihistamine tablet use in the treatment group; there was no significant change in tablet use in the control group. Response to the histamine-reducing diet varied, which was expected because diet is just one of several inciting factors in chronic urticaria and angioedema.

The small sample size and large within-and-between subject variation resulted in a significant difference in antihistamine intake between the control group and the treatment group at baseline. This difference was accounted for with the RM ANOVA; however, further studies are required to expand on these findings.

The activity of DAO and histamine metabolism can be measured (1,2). Correlating the effectiveness of the histamine-reducing diet with the patient's histamine metabolism would be interesting. Measurement of histamine metabolism may be a useful clinical test, permitting appropriate prescription of the diet.

RELEVANCE TO PRACTICE

Urticaria and angioedema patients are often desperate for relief from their symptoms. The histamine-reducing diet may benefit some of these patients. This diet is relatively easy to follow, is nutritionally adequate, and produces immediate results. A trial of dietary intervention should therefore be considered as a possible adjuvant treatment for chronic urticaria and angioedema.

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