

Idiopathic anaphylaxis: long-term follow-up, cost, and outlook

Krasnick J, Patterson R, Harris KE. Idiopathic anaphylaxis: long-term follow-up, cost, and outlook.

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To determine the efficacy of oral corticosteroids, antihistamines, and sympathomimetics in treating patients with idiopathic anaphylaxis, the charts of 225 patients diagnosed with idiopathic anaphylaxis from 1971 to 1990 treated at a single center were reviewed. Sixty-one patients (34 females and 27 males) were available for long-term follow-up. Ages ranged from 10 to 68 years with an average of 39 years. Patients with frequent episodes were treated with a protocol of oral corticosteroids, antihistamines, and sympathomimetics. Patients with infrequent episodes were treated for acute episodes only. The number of emergency room visits, hospitalizations, intensive care unit admissions, and length of time in remission were recorded. Sixty-five percent of patients with infrequent episodes and 91% of patients with frequent episodes of idiopathic anaphylaxis went into remission. Significant decreases in emergency room visits occurred for the idiopathic anaphylaxis-generalized-frequent group ($P < 0.016$), the idiopathic anaphylaxis-generalized-infrequent group ($P < 0.0001$), and the idiopathic anaphylaxis-angioedema-infrequent group ($P < 0.039$). Significant decreases in the number of hospitalizations ($P < 0.022$) and intensive care unit admissions ($P < 0.009$) occurred for the idiopathic anaphylaxis-generalized-infrequent and frequent groups, respectively. Overall, an estimated \$184 740 was saved with the treatment program, for 546 patient-years. Idiopathic anaphylaxis can be controlled and remission induced in most patients. An estimated \$11 million per year can be saved for patients in the USA on the basis of the estimated prevalence in this country.

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Key words: allergic reaction; anaphylaxis; idiopathic anaphylaxis; ketotifen.

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Accepted for publication 7 May 1996

Anaphylaxis is an immediate, life-threatening, systemic reaction mediated by bioactive substances released by mast cells and basophils. Symptoms include diffuse urticaria, gastrointestinal disturbances (vomiting, diarrhea, and abdominal cramps), bronchospasm, angioedema, airway obstruction, hypotension, cardiovascular collapse, and even death (1). Known anaphylactic episodes have occurred after ingestion of drugs, i.e., antibiotics (2); aspirin, and nonsteroidal medications (3); with latex exposure (4); after administration of radiocontrast media (5); and after Hymenoptera stings (6). Other causes of anaphylaxis include food-induced anaphylaxis (7), exercise-induced anaphylaxis (8), and food-dependent, exercise-induced anaphylaxis (9). However, there remains a group of patients for whom no known cause of anaphylaxis can be found.

Anaphylaxis with no external allergens is termed "idiopathic anaphylaxis". We have estimated that approximately 33 000 cases of idiopathic anaphylaxis exist in the USA (10). We have had the opportunity at Northwestern University to evaluate patients with idiopathic anaphylaxis over a more than 20-year period of time. During this time, we have developed classification and treatment programs for the management of patients with idiopathic anaphylaxis.

Orfan et al. previously reported this institution's experience with 225 patients found to have idiopathic anaphylaxis, with a limited long-term follow-up of 20 patients (11). After an extensive evaluation, those diagnosed with idiopathic anaphylaxis were found to have no other disease or condition explaining the recurrent episodes of anaphylaxis. Patients were managed with a protocol of oral

corticosteroids, oral sympathomimetics, and oral antihistamine medications. There were no reported fatalities attributed to idiopathic anaphylaxis in this study; however, deaths from idiopathic anaphylaxis have been reported (12, 13). We have seen additional patients with idiopathic anaphylaxis, and our service totals over 350 patients.

In this study, we retrospectively evaluated the charts of the 225 patients previously reported, and attempted to telephone them to inquire about their current disease status. Although other groups have reported series of cases of idiopathic anaphylaxis (14, 15), the current study is the largest and longest follow-up study of idiopathic anaphylaxis patients to be reported.

Material and methods

Subjects

The charts of 225 patients evaluated by the members of the Northwestern University Allergy-Immunology Division in 1971-90 and diagnosed as having idiopathic anaphylaxis were reviewed. Orfan et al. previously reported the extensive evaluation of these same patients including history, physical examination, serologic tests, radiologic tests, skin testing for food allergens and aeroallergens, and metabisulfite and tartrazine challenges (11).

Patients were classified at presentation by type and frequency of symptoms (Table 1). After patients were evaluated and their classification determined, they were instructed on the significance and severity of anaphylaxis and on emergency procedures. Patients were treated according to a previously established protocol with prednisone, hydroxyzine, and albuterol (Table 2) (11). Patients who were not able to discontinue prednisone were considered to be corticosteroid dependent and were given a trial of either oral cromolyn (Gastrocrom®) 200 mg, four times daily, and/or another mast-cell stabilizer (ketotifen), 2 mg, up to four times per day; and an additional attempt was made to discontinue prednisone (16).

Patients were initially seen weekly until they were taking prednisone on alternate days, and then they were seen approximately once a month. Prednisone was tapered according to symptoms and number of episodes. Some episodes of urticaria or angioedema, although not always life-threatening or considered frank anaphylaxis, were considered evidence of disease activity and influenced the rate of reduction of prednisone. Increases in prednisone dosage were sometimes required to control symptoms.

After careful review of the patients' charts, those patients who had a clinical course that was not

Table 1. Classification of idiopathic anaphylaxis

Idiopathic anaphylaxis-generalized-infrequent (IA-G-I)	Urticaria or angioedema with bronchospasm, hypotension, syncope, or gastrointestinal compromise with infrequent episodes (<6 episodes/year)
Idiopathic anaphylaxis-generalized-frequent (IA-G-F)	Same as above but with frequent episodes (≥ 6 episodes/year)
Idiopathic anaphylaxis-angioedema-infrequent (IA-A-I)	Urticaria or angioedema with upper airway compromise such as laryngeal edema, or massive tongue edema without other systemic manifestations and with infrequent episodes (< 6 episodes/year)
Idiopathic anaphylaxis-angioedema-frequent (IA-A-F)	Same as above but with frequent episodes (≥ 6 episodes/year)

Table 2. Treatment protocol for idiopathic anaphylaxis

Acute episode	Epinephrine 0.3 cc of 1:1000 solution subcutaneously, prednisone 60 mg orally, antihistamine (hydroxyzine 25 mg, diphenhydramine 50 mg, or chlorpheniramine 4 mg) orally. Proceed to nearest emergency room.
Infrequent episodes	Same as for acute episode
Frequent episodes	Prednisone 60-100 mg orally for 1 week or until signs and symptoms are controlled; then convert to alternate-day prednisone, 60-100 mg, cautiously tapering by no more than 5-10 mg per month. Continuous antihistamine and sympathomimetic agents

typical of idiopathic anaphylaxis, and who lacked objective evidence of symptoms, were excluded (17). Patients who were noncompliant and were discharged from the clinic were also excluded. One physician attempted to telephone all other patients. Patients that had moved or had no forwarding address or telephone number were not included in the study.

A patient's clinical history, number of emergency room visits, and hospitalizations and intensive care admissions with and without need for intubation and mechanical ventilation, before and after being cared for by our allergy service, were recorded.

Once contacted, the patients were asked about their current disease activity, including the length of time since the last episode, medications, and the number of hospitalizations, intensive care unit admissions, and emergency room visits required. Some symptoms, whether life-threatening or not, such as isolated urticaria or angioedema or gastrointestinal symptoms, were considered disease activity, and they were considered flares of idiopathic anaphylaxis if they required extra prednisone, epinephrine, or an emergency room evaluation, or if the patient's prednisone dose could not be reduced or had to be increased.

Treatment costs

The costs of both emergency care and hospitalization for idiopathic anaphylaxis were estimated on the basis of costs of services at Northwestern Memorial Hospital during the year 1995. The cost of an emergency room evaluation included nursing and physician fees, medications (intravenous corticosteroids, subcutaneous epinephrine, and intramuscular diphenhydramine), pulse oximetry, and cardiac monitoring at the Northwestern Memorial Hospital Emergency Department. The cost of a general medical floor hospital admission and intensive care unit admission with and without need of intubation and mechanical ventilation was estimated with the aid of the Northwestern Memorial Hospital Financial Department's discharge charge codes for hospitalized patients. Costs of general medical floor admissions were estimated for a 1-day admission. Intensive care unit admission included 1 day in the intensive care unit plus 1 day on the general medical floor.

Statistics

Optimal discriminant analyses (ODA) were used to determine whether the treatment protocol made a significant decrease in emergency room visits, hospitalizations, and intensive care unit admissions separately for each group of idiopathic anaphylaxis (18). Analyses were directional, and a sequentially rejective Sidak Bonferroni-type multiple-comparisons procedure was used to ensure an experiment-wise type I error rate of <0.05 .

Results

One hundred and sixty charts of 225 idiopathic anaphylaxis patients previously evaluated were retrieved from the medical records department and were available for review. Twelve patients were excluded (seven were excluded for noncompliance; five had atypical, nonobjective complaints and/or psychiatric diagnoses explaining their symptoms). Eighty-seven patients had moved without giving a forwarding address. Sixty-one patients were contacted and included in the study. Table 3 shows the patient characteristics in terms of age, sex, and classification of idiopathic anaphylaxis.

The total number of emergency room visits, hospitalizations, and intensive care unit admissions sharply decreased after patients were evaluated and treated by our service (Figs. 1 and 2). All groups had statistically significant fewer emergency room visits except the idiopathic anaphylaxis-angioedema-frequent group (Tables 4 and 5). Although the idiopathic anaphylaxis-generalized-

Table 3 Demographics of idiopathic anaphylaxis patients

Time since initial evaluation to follow-up	3.2–23.7 years
Age range	10–68 years
Average age	39 years
Females	34
Males	27
Idiopathic anaphylaxis-angioedema-frequent*	8
Idiopathic anaphylaxis-angioedema-infrequent	13
Idiopathic anaphylaxis-generalized-frequent*	20
Idiopathic anaphylaxis-generalized-infrequent	15

* Three patients were initially diagnosed as having idiopathic anaphylaxis-angioedema-infrequent but developed frequent episodes of anaphylaxis and were classified as idiopathic anaphylaxis-angioedema-frequent.

* Two patients were initially diagnosed as having idiopathic anaphylaxis-generalized-infrequent but developed frequent episodes of anaphylaxis and were classified as idiopathic anaphylaxis-generalized-frequent.

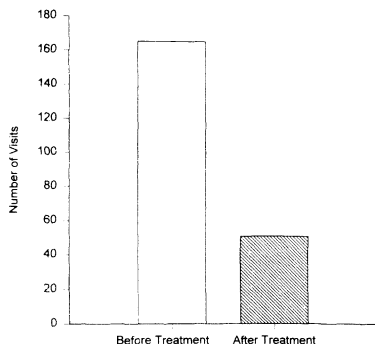


Fig. 1. Emergency room visits for idiopathic anaphylaxis before and after starting therapy.

frequent group had a trend of decreased hospitalizations (seven before and one after treatment), only the idiopathic anaphylaxis-generalized-infrequent group had a statistically significant decrease in hospitalizations ($P < 0.022$). Only the idiopathic anaphylaxis-generalized-frequent group had sufficient variability in data of intensive care unit admissions to warrant statistical analysis, which showed a significant decrease before and after starting treatment ($P < 0.009$). Data for hospitalizations for the idiopathic anaphylaxis-angioedema-infrequent group and intensive care unit admissions for the idiopathic anaphylaxis-angioedema-frequent, idiopathic anaphylaxis-angioedema-infrequent, and idiopathic anaphylaxis-generalized-infrequent groups did not have sufficient variability to warrant statistical analysis.

The estimated cost of an emergency room evaluation was approximately \$680, and the cost of admission to a general medical floor for idiopathic anaphylaxis was estimated to be \$1860 per day. The cost of admission to an intensive care unit plus 1 day on the general medical floor for idiopathic

anaphylaxis was estimated to be \$3730. The cost of admission to the intensive care unit requiring intubation and mechanical ventilation plus 1 follow-up day on the general medical floor was estimated to be \$6230.

Overall, there were 165 emergency room evaluations, 17 hospitalizations, and 18 intensive care unit admissions (five requiring intubation) for patients before being cared for by our service at a cost of \$225 000. There were 51 emergency room visits, three hospitalizations, and no intensive care unit admissions after evaluations and treatment by our service at an estimated cost of \$40 260, for a savings of \$184 740. This estimated savings of \$184 740 for 546 patient-years averages \$338 per patient-year. Applying these values to the estimated 33 000 patients with idiopathic anaphylaxis in the USA shows that an estimated \$11 154 000 dollars per year could be saved.

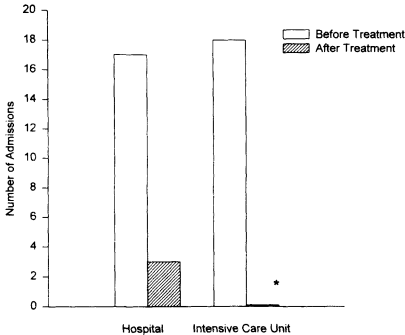


Fig. 2. Hospital and intensive care unit admissions for idiopathic anaphylaxis before and after therapy. Asterisk indicates there were no intensive care unit admissions after starting therapy.

Remission

Remission is defined as no episodes of idiopathic anaphylaxis requiring prednisone or epinephrine for at least 1 year. Overall, 65% (17) of patients with frequent episodes are in remission. Ninety-one percent (32) of patients with infrequent episodes are in remission. Those patients in remission as well as length of time in remission are shown in Tables 4 and 5.

Table 4A. Summary of data of idiopathic anaphylaxis-generalized-frequent patients

Patient no	Before/after treatment			Follow-up (years)	Status	Remission (years)	Medications	Comments
	ER	Hospital	ICU					
1	2/0	0/0	2/0	7.10	P	4.3	H	Intubated twice before therapy
2	5/0	0/0	0/0	7.11	R	2	H	
3	1/3	0/0	0/0	8.3	R	4.3	None	
4	7/0	0/0	1/0	8.10	R	8.2	None	Intubated once before therapy
5	5/0	0/0	1/0	11.11	R	11.5	H	
6	3/0	1/0	0/0	7.19	R	6.3	H	
7	4/3	3/1	2/0	9.6	R	1.9	H/G	
8	3/1	0/0	0/0	5.7	R	2	None	
9	0/0	0/0	0/0	5.2	R	2.6	H	
10	6/1	0/0	6/0	8.10	R	8.8	H	Initially IA-G-I
11	2/0	1/0	0/0	5.11	NR	—	None	
12	1/4	0/0	0/0	18.4	NR	—	H	CSD-IA
13	6/4	0/0	0/0	7.2	NR	—	None	
14	5/9	2/0	3/0	8.7	NR	—	K/H	Previously MIA
15	1/0	0/0	0/0	4.6	NR	—	H	Previously MIA, no steroids for 6 months
Total	51/25	7/1	15/0					
Mean	3.4/1.7	0.47/0.07	1/—					
SD	2.2/2.6	0.9/0.26	1.69/—					
P	0.016	0.164	0.009					

Abbreviations defined in Table 4B notes.

Table 4B Summary of data idiopathic anaphylaxis-angioedema-frequent patients

Patient no	Before/after treatment			Follow-up (years)	Status	Remission (years)	Medications	Comments
	ER	Hospital	ICU					
1	2/2	0/0	0/0	4.7	R	3.1	None	
2	30/1	1/0	0/0	21.5	R	4.7	None	
3	1/1	0/0	0/0	11.1	R	8.3	None	
4	1/0	0/0	0/0	9.2	R	3.2	None	
5	0/0	0/0	0/0	6.5	R	1	H	Initially IA-A-I
6	3/1	0/0	0/0	14.7	R	1.7	H	
7	1/0	0/0	0/0	8.5	R	2	H	
8	1/0	1/0	0/0	6.2	NR	—	C/H	
9	1/3	0/0	0/0	15.4	NR	—	C/S/H	CSD-IA, previously MIA
10	5/0	0/0	0/0	9.10	NR	—	C/H	CSD-IA
11	1/2	0/2	0/0	5.7	NR	—	K/H/S	Previously MIA, no steroids for 3 months
Total	46/10	2/2	0/0					
Mean	4.2/0.9	0.18/0.18	—/—					
SD	8.7/1	0.4/0.6	—/—					
P	0.12	0.62	*					

Abbreviations: ICU = intensive care unit, R = remission, NR = not in remission, CSD-IA = corticosteroid dependent idiopathic anaphylaxis, MIA = malignant idiopathic anaphylaxis, C = corticosteroids, H = hydroxyzine, K = ketotifen, S = sympathomimetic, G = Gastrocrum[®], P = P value. * indicates P value not calculated due to insufficient variability in data

Table 5A Summary of data idiopathic anaphylaxis-angioedema-infrequent patients

Patient no	Before/after treatment			Follow-up (years)	Status	Remission (years)	Medications	Comments
	ER	Hospital	ICU					
1	4/1	0/0	0/0	5.9	R	2	H	Hypertension
2	2/0	0/0	0/0	5.2	R	5	None	Allergic rhinitis
3	0/0	0/0	0/0	3.2	R	1.5	None	Hypertension
4	1/1	0/0	0/0	5.6	R	4	None	
5	1/7	0/0	0/0	5.1	R	4.4	H	
6	1/0	0/0	0/0	5.9	R	5.3	None	Sarcoidosis
7	1/0	0/0	0/0	6.1	R	6.1	None	
8	0/1	0/0	0/0	4.9	R	4	None	
9	5/0	0/0	0/0	11.7	R	8.8	None	
10	1/0	0/0	0/0	10.3	R	10.4	None	
11	1/1	1/0	0/0	6.1	R	5.4	None	
12	3/0	0/0	0/0	8.8	R	8.5	None	Cerebral palsy
13	1/1	0/0	0/0	12.4	R	3	None	Allergic rhinitis
14	0/1	0/0	0/0	12.4	NR	2 months	H	
15	8/1	0/0	0/0	5.5	NP	6 months	None	
Total	29.8	1/0	0/0					
Mean	1.9/0.5	0.07	—/—					
SD	2.2/1.5	0.26	—/—					
P	0.039	*	*					

Abbreviations defined in Table 5B notes

Ketotifen

Eleven patients with corticosteroid-dependent idiopathic anaphylaxis were given a trial of ketotifen, a mast-cell stabilizing agent. Five patients were classified as idiopathic anaphylaxis-generalized-

frequent, five as idiopathic anaphylaxis-angioedema-frequent, and one as idiopathic anaphylaxis-generalized-infrequent. Of these patients, four are in remission with two patients taking no medications and two patients taking antihistamines only. Of the remaining seven patients that are not

Table 5B. Summary of data of idiopathic anaphylaxis-generalized-infrequent patients

Patient no	Before/after treatment			Follow-up (years)	Status	Remission (years)	Medications	Comments
	ER	Hospital	ICU					
1	3/0	0/0	0/0	8.4	R	7.1	H	Asthma
2	3/0	0/0	0/0	23.7	R	10	None	Peanut anaphylaxis
3	2/0	0/0	0/0	7.3	R	6.3	None	Asthma, allergic rhinitis
4	7/0	3/0	0/0	7.10	R	7.4	None	Insulin allergy
5	1/0	1/0	0/0	8.11	R	8.9	None	
6	0/0	0/0	0/0	16.7	R	14	None	Asthma, allergic rhinitis
7	1/1	0/0	0/0	10.1	R	1.2	H	ABPA
8	1/1	0/0	0/0	20.3	R	3	None	Epilepsy
9	2/1	0/0	1/0	17.1	R	6	H	
10	4/0	0/0	0/0	9.3	R	8.9	H	IBS, allergic rhinitis
11	1/0	1/0	0/0	10.7	R	8.2	H	Hypertension, MVP
12	4/0	1/0	0/0	5.2	R	5	H	
13	2/0	1/0	0/0	4.2	R	1	H	Glaucoma, hypertension
14	0/0	0/0	0/0	6.2	R	4	None	
15	1/0	0/0	0/0	11.3	R	10	None	Vasomotor rhinitis
16	1/1	0/0	0/0	6.4	R	6	None	Allergic rhinitis
17	1/3	0/0	0/0	10.11	R	6	None	Allergic rhinitis
18	1/0	0/0	0/0	6.10	R	6.3	None	Allergic rhinitis, asthma
19	2/0	0/0	0/0	4.9	R	4.4	None	Coronary artery disease
20	2/1	0/0	2/0	6.10	NR	—	C/H	Intubated twice before therapy, asthma
Total	39/8	7/0	3/0					
Mean	1.95/0.4	0.35/—	0.15/—					
SD	1.6/0.75	0.75/—	0.49/—					
P	0.0001	0.022	*					

Abbreviations: ICU = intensive care unit, R = remission, NR = not in remission, CSD-IA = corticosteroid-dependent idiopathic anaphylaxis, MIA = malignant idiopathic anaphylaxis, ABPA = allergic bronchopulmonary aspergillosis, C = corticosteroids, H = hydroxyzine, K = ketotifen, S = sympathomimetic, IBS = irritable bowel syndrome, MVP = mitral valve prolapse, P = P value, * indicates P value not calculated due to insufficient variability in data

in remission, two are still taking prednisone, two are taking ketotifen plus an antihistamine, one is taking an antihistamine alone, and two are taking no scheduled medications.

Cromolyn

Six patients with corticosteroid-dependent idiopathic anaphylaxis were given oral cromolyn (Gastrocrom®). Only one patient remains on cromolyn. For all other patients, cromolyn was discontinued when no appreciable decrease in disease activity was found.

Malignant idiopathic anaphylaxis

Four patients were considered to have malignant idiopathic anaphylaxis (MIA), defined as illness requiring at least 60 mg of prednisone on alternate days or 20 mg of daily prednisone to control symptoms of idiopathic anaphylaxis for at least 2 months (19). There were no reported fatalities in this high-risk group. Of the four patients, none are still considered to have MIA; however, none are in remission. One patient is still taking prednisone and has corticosteroid-dependent idiopathic

anaphylaxis, two are taking ketotifen and are off daily or alternate-day prednisone, and one is taking only hydroxyzine, and is using the emergency protocol for acute episodes.

Discussion

Idiopathic anaphylaxis is a life-threatening, often misdiagnosed disease which is frightening and frustrating for both the patient and physician. Patients often resort to seeking opinions from various doctors and often lack information and treatment. In our more than 20 years' experience of patients with idiopathic anaphylaxis, there has been only one documented fatality related to idiopathic anaphylaxis (12). Fatal and near fatal cases have been reported (12, 13).

There are various mechanisms of anaphylaxis, including IgE-mediated anaphylaxis, where a definite external antigen is involved, as in food anaphylaxis. Other mechanisms of anaphylaxis include non-IgE-mediated reactions, or pseudo-allergy, such as radiocontrast-media reactions. No external allergen is found in idiopathic anaphylaxis, and it can be considered an endogenous type of anaphylaxis.

Several theories of the mechanism of idiopathic anaphylaxis, including activation of a subpopulation of mast cells, dysregulation of cytokines including uncontrolled release of histamine-releasing factors, or loss of histamine inhibitory factors, have been proposed. The existence of an IgG antibody against an IgE antibody has also been proposed but not proven (20). More research in this area is greatly needed to define the exact mechanism of the disease.

Our classification system and empiric treatment protocol have proven to be both cost-effective and efficient in putting the disease into remission. Cromolyn was not found to be effective in controlling frequent episodes of idiopathic anaphylaxis in corticosteroid-dependent patients and is now rarely used by our service. Ketotifen was effective in reducing the amount of prednisone and in some patients allowed complete discontinuation of prednisone.

Overall, we were able to induce a remission in 65% of patients with frequent episodes of idiopathic anaphylaxis, and in 91% of those with infrequent episodes. There are several explanations of such a high remission rate for the infrequent patients. One reason could be that patients, after a period of time, spontaneously go into remission. Secondly, it is possible that with aggressive treatment of acute episodes of idiopathic anaphylaxis, the episodes diminish in both intensity and frequency, and over time the bioactive mediators involved diminish in activity, allowing spontaneous remission to occur. Finally, a number of patients in remission are still on daily antihistamines, which may be keeping disease activity under control. A control group of patients receiving placebo has not been studied since we feel that withholding effective medications for a life-threatening disease would be unethical.

The greatest clinical benefit was observed in the idiopathic anaphylaxis-generalized groups (both infrequent and frequent classifications) with significant decreases in both groups for emergency room visits. Significant decreases also occurred in the number of hospitalizations and intensive care unit admissions for the idiopathic anaphylaxis-generalized-infrequent and idiopathic anaphylaxis-generalized-frequent groups, respectively. Although there were trends to reduction of emergency room visits and hospitalizations including intensive care unit admissions for the idiopathic anaphylaxis-angioedema-frequent group and for hospitalizations for the idiopathic anaphylaxis-generalized-frequent group, these were not statistically significant.

The amount of health-care resources utilized for the treatment of idiopathic anaphylaxis was markedly reduced after patients were seen by our

service and were treated under our regimen. Besides providing effective therapy and inducing remission in patients, the establishment of a doctor-patient relationship with easy accessibility to a physician for advice may reduce the frequency of patients using the emergency room as their primary care provider for treatment of anaphylaxis. Patients were equipped with emergency medication enabling them to suppress an attack early, sometimes negating the need for emergency room care and hospitalization. With our protocol, we were able to save over \$184 000 in emergency room visits, hospitalizations, and intensive care unit admissions for 61 patients. The saving is extensive (approximately 11 million dollars) when estimates are applied to the whole US population of idiopathic anaphylaxis patients.

A comprehensive program of education, available physicians, and appropriate therapy with prednisone, antihistamines, and sympathomimetics has proven to be effective both in reducing episodes of idiopathic anaphylaxis and in improving the quality of life for the patients, but it also decreases the amount of money spent on emergency room visits and hospitalizations.

Acknowledgments

We thank Dr Paul Yarnold for carrying out the statistical analysis. This study was supported by the Ernest S. Bazley Grant to Northwestern Memorial Hospital and the Northwestern University Medical School.

References

- McGrath KG. Anaphylaxis. In: Patterson R, Grammer LC, Greenberger PA, Zeiss CR, editors. *Allergic diseases: diagnosis and management*. 4th ed. Philadelphia, PA: JB Lippincott, 1993:587-610.
- Sullivan TJ. Drug allergy. In: Middleton E Jr, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, Busse WW, editors. *Allergy: principles and practice*. 4th ed. St Louis, MO: Mosby-Year Book, 1993:1726-46.
- Stevenson DD. Diagnosis, prevention, and treatment of adverse reactions to aspirin and non-steroidal anti-inflammatory drugs. *J Allergy Clin Immunol* 1984;74:617-22.
- Sussman GL, Beezhold DH. Allergy to latex rubber. *Ann Intern Med* 1995;122:43-6.
- Greenberger PA. Contrast media reactions. *J Allergy Clin Immunol* 1984;74:600-5.
- Reisman RE. Insect stings. *N Engl J Med* 1994;331:523-7.
- Sachs MI, Yunginger JW. Food-induced anaphylaxis. *Immunol Allergy Clin North Am* 1991;11:743-55.
- Sheffer AL, Austen KE. Exercise-induced anaphylaxis. *J Allergy Clin Immunol* 1984;73:699-703.
- Horan RF, Sheffer A. Food-dependent exercise-induced anaphylaxis. *Immunol Allergy Clin North Am* 1991;11:757-66.
- Patterson R, Hogan MB, Yarnold PR, Harris KE. Idiopathic anaphylaxis: an attempt to estimate the incidence in the United States. *Arch Intern Med* 1995;155:869-71.
- Orfan S, Stoloff RS, Harris KE, Patterson R. Idiopathic

- anaphylaxis: total experience with 225 patients. *Allergy Proc* 1992;13:35-43.
12. Krasnick J, Patterson R, Meyers G. A fatality from idiopathic anaphylaxis. *Ann Allergy Asthma Immunol* 1996;76:376-8.
13. Patterson R, Clayton DE, Booth BH, Greenberger PA, Grammer LC, Harris KE. Fatal and near fatal anaphylaxis. *Allergy Proc* 1995;6:103-8.
14. Khan DA, Yocum MW. Clinical course of idiopathic anaphylaxis. *Ann Allergy* 1994;73:370-4.
15. Tejedor MA, Perez C, De La Hox B, Jauregui I, Puras A, Alvarez-Cuesta E. Idiopathic anaphylaxis: clinical differences [Abstract]. *J Allergy Clin Immunol* 1992;89:349.
16. Patterson R, Stoloff RS, Greenberger PA, Grammer LC, Harris KE. Algorithms for the diagnosis and management of idiopathic anaphylaxis. *Ann Allergy* 1993;71:40-4.
17. Choy AC, Patterson R, Patterson D, et al. Undifferentiated somatoform idiopathic anaphylaxis: non-organic symptoms mimicking idiopathic anaphylaxis. *J Allergy Clin Immunol* 1995;96:893-900.
18. Yarnold PR, Soltysik RC. Theoretical distributions of optima for univariate discrimination of random data. *Decis Sci* 1991;22:739-52.
19. Stoloff RS, Orfan N, Greenberger PA, Grammer LC, Harris KE, Patterson R. Malignant idiopathic anaphylaxis: three additional cases and extended evaluation. *Ann Allergy* 1992;69:37-42.
20. Patterson R, Greenberger PA, Grammer LC, Zeiss CR, Harris KE, Shaughnessy MA. Idiopathic anaphylaxis (IA): suggested theories relative to the pathogenesis and response to therapy. *Allergy Proc* 1993;14:365-7.

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