

Anaphylaxis Diagnosis and Treatment at an Emergency Department in Puerto Rico

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Objective: Anaphylaxis is a severe, potentially life-threatening systemic allergic reaction. Most cases of anaphylaxis are encountered and managed at Emergency Departments (ED). We aimed to evaluate all cases of anaphylaxis and of acute allergic reactions presenting to the ED of the Veterans Affairs Caribbean Healthcare System (VACHS) to assess each patient's presentation, the possible cause of that individual's allergic reaction or anaphylaxis, and the treatment or treatments that that person received.

Methods: We conducted a retrospective review of all of the cases seen at the ED from July 2007 through July 2009 in which a diagnosis of either anaphylaxis (ICD-9-CM 995.0) or allergic reaction (ICD-9-CM 995.3) was made. We reviewed the diagnosis of each case using the anaphylaxis guidelines and compared the presentations, causes, treatments, and outcomes of patients with recognized or unrecognized anaphylaxis.

Results: The study included 135 adults. Six patients (4.4%) were diagnosed with anaphylaxis and 129 patients (95.6%) were found to have been suffering from allergic reactions. Among the patients diagnosed with allergic reactions, 25 (23%) met the diagnostic criteria for anaphylaxis but were not recognized as having experienced it. The most common causes for anaphylaxis were food (41.9%), medication (38.7%), and insect bites or stings (12.9%); in 12.9% of the cases, a cause could not be determined. There were no statistically significant differences between groups in terms of demographics, causes, or symptoms. Significant differences were found in patient vital signs upon ED arrival. There was under-treatment, particularly among subjects with unrecognized anaphylaxis. Only 67% of recognized and 4% of unrecognized anaphylaxis were treated with epinephrine ($p < 0.001$). It was more likely for subjects whose anaphylaxis was recognized to be admitted than was the case for patients whose anaphylaxis went unrecognized or who were merely suffering from allergic reactions ($p < 0.001$).

Conclusion: Anaphylaxis is under-diagnosed and under-treated in ED patients receiving care at the VACHS. There is a need to improve anaphylaxis recognition and treatment in the ED setting and, in addition, to better identify barriers to optimal health care. [*PR Health Sci J* 2013;4:170-174]

Key words: Anaphylaxis, Puerto Rico, Emergency Department

Anaphylaxis is a severe, life threatening, unanticipated systemic allergic reaction that occurs after the release of histamine and other substances from mast cells and basophils (1, 2). The incidence of anaphylaxis is unknown, but its prevalence is estimated to range from 0.05% to 2% in the general population. Food allergies and insect bites/stings are the most common causes of anaphylaxis. Approximately 50 insect bite-/sting- and 100 food-related deaths are reported each year in the United States. Less common causes include allergies to latex and medications (3). Asthmatics are particularly at risk of anaphylaxis (4). Symptoms are multi-systemic and may include laryngeal edema, lower airway obstruction, hypotension, and skin involvement with hives, angioedema, erythema or pruritus. Given the myriad of systemic symptoms and different presentations, diagnosing anaphylaxis can be a challenge for the clinician.

In 2006, the Second Symposium of NIAID/FAAN developed specific diagnostic criteria to aid the clinician in the diagnosis and management of anaphylaxis (5). Management involves the administration of an intramuscular epinephrine injection, the avoidance of the causative substance, observation, and an allergist referral. International publications have reported that anaphylaxis is often under-recognized and under-treated (6).

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The vast majority of anaphylaxis diagnoses are made in the emergency room. Studies have reported that most anaphylaxis cases are encountered and managed by ED physicians as opposed to any other physician or individual not in the healthcare industry, because of the spontaneous and sometimes unpredictable nature of the disease. However, of those patients who are managed at an ER, few are discharged with epinephrine auto-injectors and even fewer receive an allergist referral (7).

Our hypothesis is that anaphylaxis is under-diagnosed and under-treated. To test this hypothesis, we evaluated the medical records of patients who visited the VACHS Emergency Department for allergies or anaphylaxis so that we could determine which cases met the diagnostic criteria for anaphylaxis, what the most common presentation was, what the possible cause or causes might have been, and what treatment or treatments these individuals received.

Methods

Participants and setting

We conducted a retrospective study of all patients who presented to the Veterans Affairs Caribbean Healthcare System Emergency Department (July 2007 - July 2009) with a diagnosis of anaphylaxis (ICD-9-CM diagnosis code 995.0) or acute allergic reaction (ICD-9-CM 995.3). The Veterans Affairs Hospital is open 24 hours, 7 days a week, serves Puerto Rico and the US Virgin Islands, and reports 35,000 to 36,000 visits per year from a client population that consists primarily of males (97:3) (8).

Design and variables

Electronic medical records were reviewed. Information gathered from the records included demographic information (age, sex, source of referral), symptoms and signs at ED, causes of anaphylaxis as identified in the record (insect bites/stings, drugs, food, latex, idiopathic), treatment received at the ED and upon discharge (epinephrine, steroids), and outcome of the visit (including discharge home, admission, intensive care admission, intubation, or death).

We used the NIAID/FAAN criteria to determine whether the criteria for anaphylaxis were met in each case examined (5). Subjects who fulfilled any of the 3 criteria for anaphylaxis were reclassified as being unrecognized anaphylaxis cases. An experienced American Board of Allergy and Immunology-certified physician reviewed each case blindly. Briefly stated, the presence of 2 or more organ-system involvement or of hypotension upon exposure to a known allergen was consistent with the diagnosis of anaphylaxis. The systems and their associated symptoms examined included the following:

1. Skin/mucosal: generalized hives, pruritus, angioedema, flushing
2. Respiratory: dyspnea, wheeze, bronchospasm, stridor, cough, hypoxemia

3. Vascular: hypotonia, collapse, presyncope, sudden weakness, syncope, incontinence

4. Gastrointestinal symptoms: crampy abdominal pain, nausea, vomiting, diarrhea.

Statistical methods

Descriptive data are presented as frequencies, percentages, means, and standard deviations. Vital signs including blood pressure, heart rate, and oxygen saturation were compared between subjects with recognized anaphylaxis, unrecognized anaphylaxis, or allergy by performing one-way ANOVA. The *F*-statistic values obtained in ANOVA were used to calculate *p*-values to determine statistically significant differences in vital signs between the members of each group. Data from categorical variables including symptoms, causes, treatments, and outcomes were cross-tabulated and compared between study groups using the chi-square test or, when appropriate, Fisher's exact test. The *p*-values for these comparisons were calculated based on the degrees of freedom and the chi-square test statistic values obtained. A *p*-value less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 19.0.

Results

We examined all cases diagnosed with allergic reaction or anaphylaxis at the VA Caribbean Healthcare System ED from 2007 through 2009, which cases totaled 140 subjects. Five subjects did not present the signs or symptoms of an allergic condition or anaphylaxis and were excluded from the analysis. The mean age of the remaining 135 patients was 62±14.3 years (23-93 years). Most of the subjects (96.3%) were male. Six patients (4.4%) were diagnosed by ED physicians as having anaphylaxis (ICD-9 995.0), while 129 patients (95.6%) were diagnosed as having suffered an allergic reaction (ICD-9 995.3). The most common causes of reactions identified at the Emergency Department were medication (58 subjects, 42.9%), food (31 subjects, 22.9%), inhalants such as grass or dust (8 cases, 5.9%), insect stings/bites (5 subjects, 3.7%), and latex (2 cases, 1.4%). The conditions for 30 subjects (22.2%) were idiopathic.

We found that 31 patients (23%) met the criteria for anaphylaxis. The 6 patients previously diagnosed as anaphylactic by the ED physicians met the criteria, as did 25 additional patients whose anaphylaxis was not recognized at the ED. We compared the demographic characteristics, symptoms, etiologies, outcomes, and treatments of the 3 groups of patients.

The mean age of the 6 patients diagnosed with anaphylaxis (ICD-9-CM 995.0) at the ED was 58.8±14.3 years. All were male patients. Subjects whose anaphylaxis was not recognized had a median age of 56.92±13.3 years; this group contained 2

female patients. The remaining 104 patients had a mean age of 63.56±14.3 years; 3 of the patients in this group were female. There were no statistically significant differences between the groups in terms of age or sex (p = 0.097, and p = 0.423, respectively).

The most common causes for anaphylaxis were food (41.9%), medication (38.7%), and insect bites/stings (12.9%); 12.9% of the conditions were idiopathic in nature. No anaphylaxis to latex was reported. There were no statistically significant differences in terms of the causes of reactions in those whose anaphylaxis was recognized and compared to those whose anaphylaxis not recognized. (p = 0.176, p = 0.426, p = 0.159, and p = 0.402). Food-associated anaphylaxis was ascribed most commonly to shrimp (4); salmon (3); seafood (2); pepperoni, applesauce, chocolate, and cookies (1 each); and undetermined foods (2). Medications associated with anaphylaxis included aspirin/NSAID (4); sulfa (2); and iron dextran and methylprednisolone, ACE inhibitors, lidocaine, radio contrast agents, and CQ-100 (1 each). Cases of anaphylaxis that were caused by insect bites/stings included 3 that resulted from bee stings and 1 that was provoked by fire ants.

In patients whose anaphylaxis was recognized at the ED versus those whose anaphylaxis was not so recognized, there were no differences in symptoms at presentation (p = 0.354 for angioedema, p = 0.641 for urticaria, p = 0.501 for reported hypotension, p = 0.235 for reported hypoxemia, p = 0.598 for wheezing, p = 0.598 for gastrointestinal symptoms, p = 0.512 for coughing, p = 0.295 for laryngeal edema).

In terms of the vital signs of patients arriving at the emergency room, statistically significant differences were found between those whose anaphylaxis was recognized, those whose anaphylaxis was unrecognized, and those who were found to be suffering from allergic reactions, as shown in Table 1. Subjects whose anaphylaxis was recognized were more likely to present with relatively lower oxygen saturation, relatively lower diastolic blood pressure, and relatively higher heart rates than were those whose anaphylaxis was not recognized or who were just allergic.

Table 1. Patient vital signs upon arrival at the Emergency Department (subjects with anaphylaxis, unrecognized anaphylaxis and allergy).

	Anaphylaxis	Unrecognized anaphylaxis	Allergy	p-value
Systolic Blood Pressure (mm Hg)	130.83±25.44	129.8±19.61	130.37±16.08	0.986
Diastolic Blood Pressure (mm Hg)	74.17±9.56	82.4±14.66	75.97±10.46	0.036
Heart rate (b/min)	92.6±10.71	87.0±15.80	77.02±13.17	0.001
Oxygen saturation (%)	93.6±5.56	97.54±2.6	97.9±1.54	<0.001

In the Emergency Department, there were significant differences in the management of patients with recognized anaphylaxis, unrecognized anaphylaxis, and allergies, as shown in Table 2. There was under-treatment of anaphylaxis, which was particularly evident among subjects whose anaphylaxis was not recognized. Only sixty-seven percent of the recognized and 4% of the unrecognized anaphylaxis patients were treated with epinephrine (p<0.001). There were significant differences in the timing of epinephrine administration between subjects with anaphylaxis. All of the subjects recognized as having anaphylaxis received immediate epinephrine, while those 2 cases that were not recognized as such received epinephrine at least 1 hour later (p<0.001). All of the subjects with recognized anaphylaxis and 88% of those with unrecognized anaphylaxis received steroids at the ED; in comparison, steroids were given to 56% of the allergic patients. There were no differences in terms of the prescribing of steroids upon discharge from the Emergency Department between groups. Ironically, none of the subjects who were recognized as suffering from anaphylaxis were referred to allergists for evaluation, unlike 28% of the unrecognized anaphylaxis patients and 11% of the allergic patients (p = 0.044).

Table 2. Outcomes and treatments of subjects who arrived at the Emergency Department (ED) with anaphylaxis, unrecognized anaphylaxis, or allergy.

	Anaphylaxis (%)	Unrecognized anaphylaxis (%)	Allergy (%)	p-value
Epinephrine at ED	4/6 (66%)	2/25 (8%)	0/104 (0%)	<0.001
Epinephrine upon arrival	4/6 (66%)	0/25 (0%)	0/104 (0%)	<0.001
Steroids at ED	6/6 (100%)	22/25 (88%)	59/104 (57%)	0.002
Steroids at discharge	3/6 (50%)	12/25 (48%)	39/104 (37%)	0.552
Allergist referral	0/6 (0%)	7/25 (28%)	11/104 (11%)	0.044
Admission to hospital	3/6 (50%)	2/25 (8%)	5/104 (5%)	<0.001

There were significant differences in the outcomes of cases as well. Those subjects whose anaphylaxis was recognized were more likely to be admitted than were those whose anaphylaxis was unrecognized or who were found to be suffering allergic reactions (p<0.001). One patient with recognized anaphylaxis was intubated and admitted to the intensive care unit. No subjects died.

Subjects with anaphylaxis were evaluated for differences in symptoms or causes of anaphylaxis by age. No significant age-based differences were found in any of the subjects, though older subjects were more likely to suffer from hives than younger subjects were (p=0.07). Older subjects with anaphylaxis were more likely to have lower diastolic blood pressures at presentation (73.11±15.14 compared to 83.95±12.65, p = 0.05).

Discussion

We identified a large proportion of patients who had received care at the Veterans Affairs Caribbean Healthcare System Emergency Department and whose anaphylaxis was both under-recognized and under-treated. Deranged vital signs, immediate epinephrine use, the increased likelihood of hospital admission, and the reduced likelihood of allergist referral were all more common for subjects whose anaphylaxis was immediately identified than they were for those subjects whose anaphylaxis remained unrecognized. These findings support the need to improve anaphylaxis recognition and treatment in the ED setting.

The National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network guidelines developed criteria to aid clinicians in the recognition of anaphylaxis (5). Still, under-diagnosis and under-treatment has been reported in many clinical settings, worldwide (6, 9). In fact, the consensus panel concluded that 1 in 20 patients were likely to be misdiagnosed (10). In our cohort, patients who were diagnosed at the ED as having anaphylaxis did, in fact, fulfill the diagnostic criteria. However, the physicians missed a large number of cases, which were diagnosed as allergic reaction (80.6%), as reported in the literature.

Sheikh reported that the lifetime prevalence of anaphylaxis varied markedly by age and sex (10). In the pre-pubertal period, lifetime prevalence was the highest in males, but then increased very rapidly in females, peaking during the fifth decade. In our cohort, most of the cases of anaphylaxis were males, which is to be expected from a VA population. We did not find significant differences in groups when analyzing by age or sex. Unlike Campbell et al., who reported that elders with anaphylaxis had more cardiovascular symptoms and were more likely to be admitted and less likely to receive an epinephrine prescription (11), we found no difference in terms of either treatment or outcome between elderly and younger adults with anaphylaxis.

Patients adequately diagnosed with anaphylaxis at the ED had significant alterations in vital signs, including lower diastolic blood pressure, more hypoxemia, and more tachycardia than were seen in other groups. The immediate use of epinephrine, higher hospitalization rates (50%), including 1 ICU admission (16%), and need for intubation suggest that the severity of the anaphylaxis symptoms of these patients was more severe than was that displayed by the patients whose anaphylaxis remained unrecognized. Nevertheless, only 66% received epinephrine at the ED and 100% received steroids. None of them was referred to an allergist, even though 2 cases presented with bee-sting anaphylaxis, for which immunotherapy is the standard of care. Thus, these patients received treatment that was suboptimal as it was not in accordance with that described in the existing guidelines. Epinephrine was used in only 3.8% of the cases

presenting with unrecognized anaphylaxis, and it was not administered immediately upon the arrival of these patients; 88% of them received steroids at the ED, and 26.9% were referred to an allergist. Our findings revealed that the most common treatment currently in use on the cohort—steroid administration—is not that which is described in the current guidelines, which guidelines stress the need for the immediate administration of epinephrine (12, 13); in fact, a Cochrane review failed to reveal any benefits whatsoever to the use of glucocorticosteroids in the emergency management of anaphylaxis (14). Paradoxically, patients whose anaphylaxis was correctly diagnosed were less likely to be referred to an allergist than was the case for those patients whose condition remained unrecognized. Campbell et al. reported that patients younger than 18 years of age were more likely to be referred to an allergist after an episode of anaphylaxis ($p = 0.007$) (15). Clark et al. reported that the percentage of patients referred to an allergist or provided with a prescription for self-injectable epinephrine on discharge from the ED was 12% but that this percentage was highly variable (16).

No fatalities were reported in our cohort. However, 1 patient required mechanical ventilation and ICU care. The literature reports low anaphylaxis mortality rates in general, although the elderly have higher rates, which rates are linked to comorbid conditions and iatrogenic drug exposures (17).

Our study has several limitations. The study is a small retrospective analysis of cases evaluated for allergy or anaphylaxis at the ED. We conducted a chart review using an electronic medical record to validate the diagnosis given. The study was conducted at the San Juan VA, a hospital whose population is mostly older male veterans and predominantly Puerto Rican, which may limit the generalization of its findings. No longitudinal data were collected to determine the effect on these subjects of the under-diagnosis of anaphylaxis.

The study has several strengths. It is unique in its description of anaphylaxis in a predominantly Puerto Rican population, demonstrating food as the most common cause (specifically crustaceans and fish). Peanut-related anaphylaxis, the most common food anaphylaxis in the United States (18), was not reported in our cohort. In terms of anaphylaxis linked to medication, our data point toward non-steroidal anti-inflammatory agents as being the most common causes, coinciding with a previous report of anaphylaxis among Puerto Ricans (19). In this study, a retrospective review of anaphylaxis cases, the most common cause of anaphylaxis was medication (39.2%), with causes that could not be identified being slightly lower (37.3%) in our cohort. Under-recognition of anaphylaxis was not reported.

The study underlines the importance of educating patients, primary care physicians, and ED staff on how to properly diagnose and treat anaphylaxis. Barriers to the appropriate identification and treatment of anaphylaxis must be evaluated in order to improve care.

Resumen

Objetivo: Anafilaxis es una reacción sistémica, severa y potencialmente fatal. La mayor parte de los casos de anafilaxis son diagnosticados y manejados en las de Sala de Emergencias (SE). Nuestra meta fue evaluar los casos de anafilaxis y alergias atendidas en el Sistema de Salud del Hospital de Veteranos (SSHV) para identificar las presentaciones, causas y tratamientos recibidos. **Métodos:** Se evaluó retrospectivamente expedientes de anafilaxis 995.0 y reacciones alérgicas 995.3 vistos en la SE de julio de 2007- julio de 2009. Se reevaluaron los diagnósticos basándonos en la guía y comparamos la presentación, causas, tratamientos y desenlace de pacientes diagnosticados o no, con anafilaxis. **Resultados:** El estudio incluyó 135 adultos. Seis pacientes (4.4%) fueron diagnosticados con anafilaxis y 129 (95.6%) como alergia. Entre estos, 25 pacientes (23%) llenaron criterios de anafilaxis, pero no fueron reconocidos. Las causas más comunes de anafilaxis fueron comidas (41.9%), medicamentos (38.7%), picadas de insectos (12.9%) o idiopáticas (12.9%). No hubo diferencias significativas entre los grupos en términos de demografía, causas o síntomas. Se encontraron diferencias significativas en los signos vitales al llegar a la SE. El tratamiento de anafilaxis fue sub-óptimo, particularmente en el grupo en que no se reconoció. Solo 67% de los diagnosticados y 4% de los no reconocidos fueron tratados con epinefrina ($p < 0.001$). Los casos de anafilaxis reconocidas se admitieron más que los no reconocidos y los alérgicos ($p < 0.001$). **Conclusiones:** Anafilaxis no se diagnostica ni se trata apropiadamente entre los pacientes de la SE del SSHV. Necesitamos mejorar el reconocimiento y el tratamiento de anafilaxis e identificar barreras al cuidado óptimo de salud.

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