Original Article

Emergency Department Management of Hereditary Angioedema Attacks: Patient Perspectives

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What is already known about this topic? Emergency department (ED) care comprises a significant portion of hereditary angioedema (HAE) management. ED management of HAE was hindered by limited treatment options until Food and Drug Administration approval of 4 on-demand HAE therapies starting in 2009.

What does this article add to our knowledge? Patient-reported data identified lack of HAE awareness and medication mismanagement as areas for improvement in the ED. Having an established, effective treatment plan appears to improve medical management of HAE in the ED.

How does this study impact current management guidelines? Although ED management of HAE attacks has improved since the development of HAE therapies, there is room for improvement with a focus on HAE awareness and administration of effective HAE therapies.

BACKGROUND: Emergency department (ED) management of hereditary angioedema (HAE) has been hindered by misdiagnosis and limited treatment options. Food and Drug Administration approval of 4 on-demand HAE therapies starting in 2009 and the publication of ED guidelines for angioedema management in 2014 should facilitate improvement of HAE management in the ED.

OBJECTIVE: The objective of this study was to identify patient-reported areas for improvement in ED management of HAE attacks.

METHODS: Patients with self-reported HAE with C1 inhibitor deficiency who attended the 2015 HAE Association Patient Summit were asked to complete an anonymous 30-question survey. Questions addressed patient characteristics and HAE management in the ED.

RESULTS: Patients indicated that understanding of HAE in the ED needed improvement (99%, 104 of 105 patients). Recognition of HAE as a diagnosis (48%, 50 of 105 patients), appreciation of HAE as a serious disease (45%, 47 of 105 patients), and medication management (59%, 62 of 105 patients) were identified as areas needing improvement. Among 39 patients who required ED care within the last year, 6 did not receive any HAE-targeted therapy, and treatment with corticosteroids (n = 3), epinephrine (n = 2), and antihistamines (n = 7) was reported. Among 68 patients whose treatment plan was to receive home on-demand therapy, 26 required ED care because of an inability to receive on-demand therapy at home as outlined in their treatment plan. Having a treatment plan was associated with a greater likelihood of receiving HAE therapy in the ED (99% vs 74%, $P = .002$).

CONCLUSION: HAE management in the ED can be improved with a focus on recognition of HAE attacks and administration of effective HAE therapies. © **2016 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2016;■:■-■)**

Key words: *Hereditary angioedema; Hereditary angioedema attacks; Treatment plan; Angioedema management; Emergency department; Angioedema guidelines; On-demand treatment; Patient-reported outcomes; Quality of life; Disease burden*

Hereditary angioedema with C1 inhibitor deficiency (HAE-C1INH) is an autosomal dominant disease with an estimated prevalence of 1/10,000 to 1/100,000.[1] In HAE-C1INH, mutations in the C1-INH gene, *SERPING1*, lead to deficiency or dysfunction of the C1-INH protein.[1,2] C1-INH protein

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I. M. Otani has received a grant to attend the 2015 Hereditary Angioedema Association Patient Summit.

Conflicts of interest: I. M. Otani has received travel support from the Hereditary Angioedema Association. P. Busse has received consultancy fees from CSL Behring and Shire; and has received research support from Shire. B. L. Zuraw has received consultancy fees from Alnylan, Arrowhead, BioCryst, CSL Behring, Dyax, Ionis, Nektar, Shire, and Salix; and has received travel support from US Hereditary Angioedema Association (HAEA). M. A. Riedl is on the US HAEA Medical Advisory Board; has received consultancy fees from Shire, Dyax, CSL Behring, Salix, Arrowhead, BioCryst, Ionis, Global Blood Therapeutics; has received research support from Shire, Dyax, CSL Behring, BioCryst, Pharming, Ionis; and has received lecture fees from Shire, Dyax, Salix, CSL Behring. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication March 30, 2016; revised June 8, 2016; accepted for publication June 28, 2016.

Available online ■■

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2213-2198

http://dx.doi.org/10.1016/j.jaip.2016.06.029

Abbreviations used
ED- Emergency department
FDA- Food and Drug Administration
HAE- Hereditary angioedema
HAE-C1INH- HAE with C1 inhibitor deficiency

deficiency or dysfunction leads to activation of the contact system with generation of bradykinin, which triggers increased vascular permeability via bradykinin-2-receptors on endothelial cells. Clinically, this translates into unpredictable, potentially life-threatening, recurrent angioedema of cutaneous (face, genitalia, extremities) and mucosal (abdomen, oropharynx, larynx) tissues that can require emergency care.[2,3] Emergency department (ED) care comprises a significant portion of HAE medical management in the United States, with prior publications reporting conservative estimates of 2282 to 5040 ED visits and 1691 to 3375 hospitalizations annually.[4-6]

HAE is a rare disorder and is often not considered in the differential of patients presenting to the ED with angioedema or recurrent abdominal pain.[7] Until recently, ED management of HAE has been hindered by misdiagnosis and limited treatment options.[8] Effective treatment of HAE attacks has become increasingly possible with the Food and Drug Administration (FDA) approval of 4 on-demand HAE therapies starting in 2009.[9] Despite advances in HAE care, a survey performed at the 2013 HAE Association Patient Summit revealed that 70% of patients with HAE in the United States were not satisfied with their ED care.[8] A recent study from outside the United States suggests that medication mismanagement and inappropriate discharge planning are areas of HAE ED management that need improvement.[10]

In 2014, ED guidelines for angioedema management, including HAE emergency care, were published.[11] These guidelines should facilitate future efforts to improve HAE care in the ED.[11] In addition, other HAE guidelines have addressed the treatment of acute attacks.[1,12,13] As HAE attacks result in significant and multifaceted disease burden, patient perspectives must be considered to ensure that efforts to improve ED HAE care also result in decreased disease burden and improved quality of life.[7] The purpose of our study was to investigate the concordance between ED HAE care and published guidelines, and to identify areas that need further improvement.

METHODS

Subjects

We recruited potential patients with HAE from across the United States in attendance at the 2015 HAE Association Patient Summit (October 9-11, Denver, Colo). Patients self-reported HAE-C1INH and were asked to complete an anonymous 30-question survey (available in this article's Online Repository at www.jaci-inpractice.org). The purpose of data collection was explained to patients by investigators. Parents recorded responses for patients 0 to 15 years of age. An Investigational Review Board waiver was granted because the data were deidentified.

Survey

The survey was developed by IMO and collaborating HAE experts (AB, MAR, SCC, PB) to characterize HAE management in the ED. The survey was created through a review of prior survey data, obtaining consensus among the authors, and a review of ED guidelines for angioedema management. Questions were categorized into several broad areas. All patients were instructed to complete the first 8 questions in the questionnaire addressing baseline patient characteristics (demographics, HAE type, emergency treatment plan).

Patients with at least one ED visit were instructed to complete questions 9 through 30. Questions 9 through 16 addressed general ED care issues (understanding of HAE in the ED and comparing ED HAE care and understanding before and after 2009) that were reported for this ED group. Questions 18 to 30 asked patients about their experiences during their most recent ED visit.

Patients who had at least one ED visit for HAE treatment during their lifetime were identified based on their answers to question 3 (answers a, b, c, and d). This group is referred to as the "ED group" throughout the article.

Question 3: How many times have you been to the emergency department (ED) for treatment of HAE?
a. Once
b. 1 to 10 times
c. 10 to 25 times
d. More than 25 times
e. I have never gone to an ED for HAE treatment

Patients who reported that their last ED visit for HAE occurred during or after 2009 were identified based on their answers to question 17 (answers a, b, and c). These patients are referred to as the "2009+ group."

Patients who reported that their last ED visit for HAE was within the last year, or after October 2014 as the survey was deployed in October 2015, were also identified based on their answers to question 17 (answer a). These patients are subsequently referred to as the "2014+ group."

Question 17: How long ago was your most recent visit to the ED?
a. Within the past year
b. Within the last 1-2 years
c. Greater than 2 years
d. Before 2009
e. I do not remember

The 2009+ group and the 2014+ group were created so that the data reported would accurately reflect changing practices of ED HAE care, as 2009 was when the first FDA-approved HAE medications became available and April 2014 was when the ED angioedema guidelines were published.[11]

The total number of patients who answered each question is shown in Table E1 (available in this article's Online Repository at www.jaci-inpractice.org). The numbers of patients who answered each question among the ED group, the 2009+ group, and the 2014+ group are also shown in Table E1.

Statistical Analysis

Statistical analyses were performed using Stata/IC 14.0 (StataCorp, College Station, Tex). Fischer's exact test or χ^2 test was used as appropriate for comparisons of proportions between 2 groups. All *P*-values were 2-tailed, with $P < .05$ considered statistically significant. Missing answers for questions were excluded from analysis.

RESULTS

Patient demographics

Patients with HAE-C1INH who completed the survey (n = 118) were representative of all age groups (0-15, 16-25,