Current Medical Management of Hereditary Angioedema (HAE): Follow-up to a Large Survey of US Clinicians

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Marc A. Riedl[1]; Aleena Banerji[2]; Richard Gower[3]

[1]University of California, San Diego, CA, US; [2]Massachusetts General Hospital, Boston, MA, US; [3]University of Washington, Spokane, WA, US

BACKGROUND

Design

- Surveys were conducted in 2010 and 2013 in the US to identify trends in clinician characteristics pertaining to hereditary angioedema (HAE), ie, diagnostic and treatment practices, factors that influence clinician and patient treatment choices, and clinician awareness of new therapies
- Analysis of the findings illustrated changes in HAE treatment paradigms over three years, including fewer HAE-related hospitalizations, significantly more patients with HAE being treated at home, greater patient satisfaction with HAE treatment, and reduced androgen usage[1,2]
- In light of the dynamic treatment landscape of HAE management and recently published consensus recommendations,[3] a third survey was conducted in 2019
- The objective of this follow-up survey was to build upon the results of the two earlier studies and further evaluate current HAE management, including the impact of new treatment options on evolving clinician practice patterns over time

METHODS

- This was a voluntary, web-based survey of US clinicians treating patients with HAE
- Potential participants were identified using mailing lists obtained from the US Hereditary Angioedema Association and the American College of Allergy, Asthma & Immunology
- During June and July 2019, 5382 clinicians were contacted via postal mail with a request to complete a 47-question online survey (hosted by SurveyMonkey®, Palo Alto, CA) closely patterned after the previous two surveys
- One follow-up reminder was sent via postal mail
- Respondents were given a $25 honorarium
- For each survey question, de-identified data were analyzed, and basic descriptive statistics were generated
- Statistical analysis was used on responses to selected questions to evaluate differences and/or trends between the three surveys

RESULTS

Data Collection

- A total of 177 clinicians responded to the survey (response rate, 3%), with 156 indicating that they treat patients with HAE **(Table 1)**
- In the 2010 and 2013 surveys, a total of 172 and 245 clinicians treating HAE responded, respectively

Prophylaxis Patterns

- Use of long-term prophylaxis appeared to vary among clinicians, though over half of respondents (63.3%) indicated that 41–100% of their patients are on long-term prophylaxis
- The factors clinicians regarded as most influential when deciding to prescribe long-term prophylaxis included attack severity, attack frequency, and a history of laryngeal attacks, and showed little variation from the previous surveys
- Across the three surveys, significant changes (P<0.001) were seen in the reported frequency of danazol (↓ from 55.8% in 2010 to 23.4% in 2013 to 6.4% in 2019) and C1-INH (↑ from 20.4% to 56.7% to 60.0%) use for long-term prophylaxis **(Figure 1)**
- The subcutaneous (SC) form, rather than the intravenous (IV) form, of C1-INH was more commonly identified in 2019 as the agent of choice for long-term prophylaxis (41.4% reported SC vs 18.6% reporting IV), though the home was reported as the most frequent setting of administration regardless of C1-INH form (74.5% of all SC and 54.2% of all IV administrations)

Table 1. *2019 demographic and practice characteristics of respondents (HAE-treating clinicians)*

Characteristic	Respondents (HAE treaters), no. (%) 2019 (n=156)*
Degree (n=148)	
MD	121 (82)
DO	10 (7)
PhD	1 (1)
MD, PhD	5 (3)
Other	11 (7)
In practice (n=147)	
<1 y	2 (1)
1–10 y	57 (39)
11–20 y	47 (32)
21–30 y	20 (14)
>30 y	21 (14)
Medical specialty (n=148)	
Allergy/immunology	146 (99)
Internal medicine	8 (5)
Family practice	1 (1)
Pediatrics	3 (2)
Other	0 (0)
Practice setting (n=148)	
Office-based, solo practice	25 (17)
Office-based, single-specialty group practice	47 (32)
Office-based, multi-specialty group practice	46 (31)
Academic medical center	30 (20)
Community hospital	0 (0)
Population size of practice location (n=148)	
<10,000	1 (1)
10,000–100,000	25 (17)
101,000–500,000	54 (37)
501,000–1,000,000	24 (16)
>1,000,000	44 (30)
No. patients with HAE treated in the past year (n=148)	
1–5	104 (70)
6–10	28 (19)
11–15	9 (6)
16–20	2 (1)
>20	5 (3)

*Not all respondents answered all questions and more than one option could be selected for some questions; thus, percentage values were calculated based on the number of respondents who answered a particular question

- The non-efficacy factor influencing clinician choice of prophylaxis agent cited most often was cost and/or insurance coverage (43.7% vs 24.4% in 2010 and 40.5% in 2013) **(Figure 2)**
- Concern over adverse effects dropped to 16.2% from 55.8% in 2010 and 29.5% in 2013 (P<0.001) for clinicians and to 10.6% from 41.9% in 2010 and 15.8% in 2013 (P<0.001) for patients (as perceived by respondents) **(Figures 2 & 3)**
- Route of administration increased in significance among clinicians to 16.9% vs 3.5% in 2010 and 6.0% in 2013 (P<0.001) and among patients (as perceived by respondents) to 11.3% vs 3.5% in 2010 and 5.4% in 2013 (P=0.004) **(Figures 2 & 3)**
- The majority, 87.5%, of clinicians indicated that they prescribe short-term prophylactic treatment in high-risk situations (ie, invasive procedures), and 72.8% responded that C1-INH remains the treatment agent of choice

Figure 1. *Long-term HAE prophylaxis, medications reported as used most frequently, 2010 vs 2013 vs 2019*

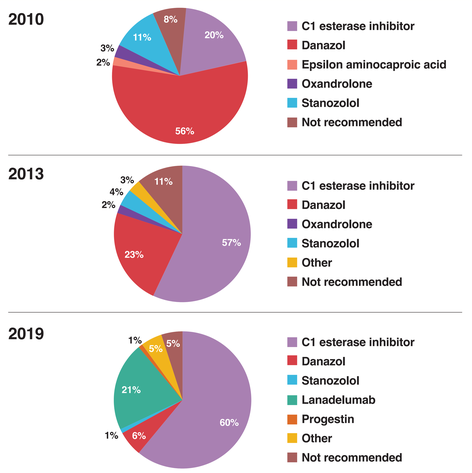
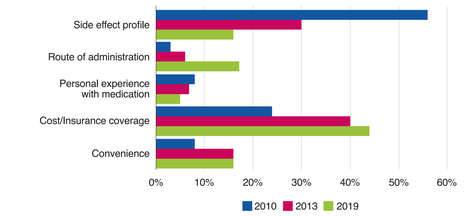


Figure 2. *Clinician reports of non-efficacy factors most important when considering long-term prophylaxis*



Management of Acute HAE Attacks

- For acute attacks, 52.9% and 31.9% of clinicians indicated they prescribe C1-INH (plasma-derived and recombinant, respectively) compared to 49.4% in 2010 and 68.9% in 2013 (for plasma-derived only, recombinant not available) **(Figure 4)**
- Icatibant was cited by 71.7% of clinicians in the management of acute attacks compared to 53.9% in 2013, an increase of statistical significance (P<0.001)

Figure 3. *Clinician perceptions of non-efficacy factors most important to patients for long-term prophylaxis*

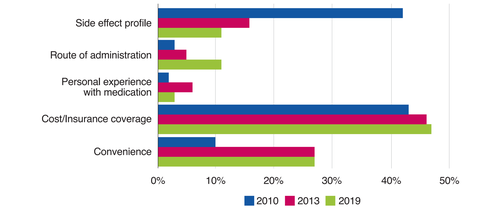
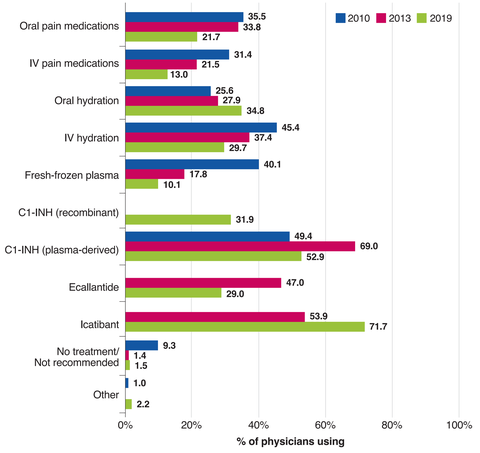
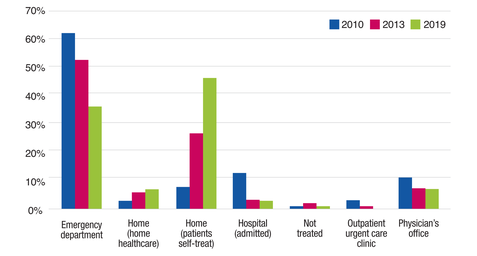


Figure 4. *Clinician-reported treatments used for acute HAE attacks, 2010 vs 2013 vs 2019 (clinicians could choose more than 1 answer)*



- Clinician-reported use of pain medication for acute attacks decreased significantly over the years (P<0.001), with the prescription of oral pain medication decreasing from 35.5% and 33.8% in 2010 and 2013, respectively, to 21.7% in 2019, and the prescription of IV pain medication decreasing from 31.4% and 21.5% to 13.0%, respectively
- Similar to 2013 (1.4%), only 1.5% of clinicians reported not prescribing treatment for acute attacks
- Treatment in the home setting (self-treatment or home healthcare) was most frequently reported and increased significantly (P<0.001) from 11.6% in 2010 to 32.5% in 2013 to 54.2% in 2019 **(Figure 5)**

Figure 5. *Clinician-reported settings for HAE attack treatment, 2010 vs 2013 vs 2019*



- The use of the emergency department for acute attack treatment decreased significantly across the years (from 61.1% in 2010 to 53.9% in 2013 to 34.8% currently; P<0.001)

Clinician-reported Patient Satisfaction

- Clinician-reported patient satisfaction with current treatment options remains high, with only 1.5% of clinicians indicating their patients are not satisfied (21.5% in 2010 and 2.7% in 2013)

Limitations

- Not all questions were answered by all respondents
- Certain questions required estimations on the part of the respondent and/or generalizations to their entire HAE population
- Outcomes should therefore be interpreted as based primarily on physician recall and/or opinion
- The respondents to this survey are not identical to the respondents from the previous surveys

CONCLUSIONS

- This updated survey reflects important developments in HAE treatment patterns among US clinicians from 2010 through 2019, consistent with published evidence-based guidelines
- C1-INH is now reported as the most frequently prescribed agent for prophylaxis, and the use of androgens as a preferred agent has decreased significantly
- The home replaced the emergency department as the most frequently reported setting for acute attacks and reported use of the emergency department among patients has decreased significantly
- Clinician-perceived patient satisfaction with treatment remains high

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