Burden of Untreated Hereditary Angioedema Attacks and its Impact on Social, Mental, and Physical Health

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Background

- Hereditary angioedema (HAE) is a rare genetic disease associated with unpredictable, painful, and debilitating attacks of tissue swelling in various locations of the body that can be life-threatening depending on the location(s) affected
- Global HAE treatment guidelines recommend that people living with HAE should consider treating all attacks early upon recognizing them in order to reduce morbidity and mortality[1-3]
- Despite availability of on-demand therapies, patients do not universally treat attacks[4]

Objective

- We examined the impact of the patients' last untreated attack on social, mental, and physical health

Methods

- The US Hereditary Angioedema Association recruited participants with Type 1 or 2 HAE between April and June 2023
  - Recruitment was stratified to include approximately 50% of participants taking on-demand only and 50% receiving non-androgen long-term prophylaxis (LTP) plus on-demand, at the time of their last treated attack
- Participants completed a 20-minute, self-reported, online survey that inquired about their last untreated HAE attack
- Participants had to be at least 18 years old and had at least 1 untreated attack in the past 3 months
- Physical and social QoL was assessed using a modified version of the Hereditary Angioedema Quality of Life Questionnaire (HAEA-QoLv2)
  - Physical impact of HAE (energy level, sleep, and activity level)
    - Range from 1 (not at all) to 4 (severe/very severe)
  - Social impact of HAE (ex. felt embarrassed, felt socially isolated)
    - Range from 1 (strongly disagree) to 5 (strongly agree)
- EuroQol Five-Dimensions Five-Levels (EQ-5D-5L), a self-report survey, was used to assess physical and mental QoL "today" (i.e., current QoL) and at the time of the last untreated attack
  - EQ-5D-5L Index Score = QoL composite of items across 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression
    - Range from −0.59 (lowest possible health state) to 1 (best possible health state)
  - Visual Analogue Score (VAS) = Single-item, self-assessment of overall health status
    - Range from 0 ("worst imaginable health state") to 100 ("best imaginable health state")

Results

Table 1. Respondent Characteristics

	Total (n=20)	On-Demand Treatment Only (n=9)	On-Demand Treatment + LTP (n=11)
Current Mean Age, Years (SD)	39 (14.6)	45 (14.2)	33 (13.1)
HAE Type			
Type 1	80%	89%	73%
Type 2	20%	11%	27%
Gender			
Female	75%	67%	82%
Race / Ethnicity			
White	87%	89%	79%
Hispanic or Latino	9%	8%	14%
Black/African American	3%	3%	7%
American Indian/Alaskan Native	2%	0%	14%
Asian	3%	4%	0%
Other	1%	1%	0%

- On-demand treatment only participants and on-demand + LTP participants both reported having an average of 10 attacks over the past year
  - On-demand treatment only participants treated 22% of attacks
  - On-demand + LTP participants treated 64% of attacks

Figure 1. Prescribed On-demand Treatment at the Time of Last Untreated Attack

On-Demand Therapy		On-demand Treatment Only (n=9)	On-demand Treatment + LTP (n=11)
Icatibant	75%	78%	73%
Plasma Derived C1 Esterase Inhibitor	30%	22%	36%

- 55% reported self-administering on-demand treatment for their attacks

Figure 2. Long-Term Prophylaxis at Time of Last Untreated Attack (n=11)

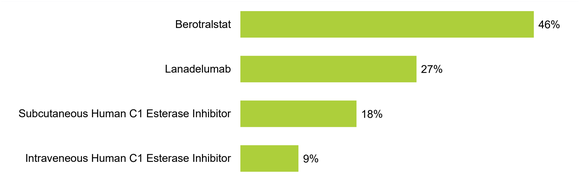
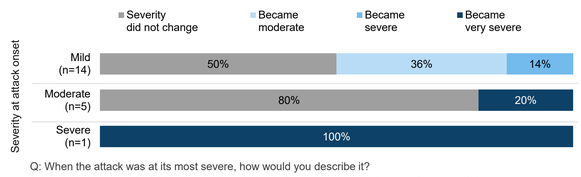


Figure 3. Progression of Untreated Attack Severity

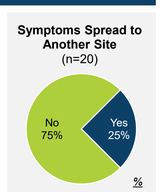


Q: When the attack was at its most severe, how would you describe it?

- 14 participants (70%) described their last untreated attack as mild at treatment and of these, 7 participants (50%) progressed to moderate/severe
- Severity progressed for 45% of all attacks, either becoming moderate, severe, or very severe

Figure 4. Initial Site of Attack and Symptom Spread

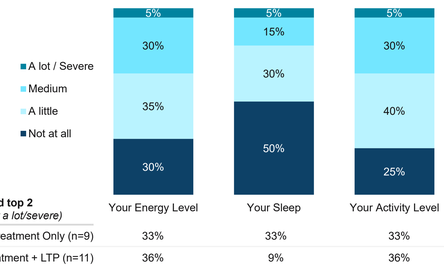
Initial Site of Attack		On-Demand Treatment Only (n=9)	On-Demand Treatment + LTP (n=11)
Peripheral / Trunk (net)	55%	78%	36%
Peripheral (e.g., hands, legs, feet, etc.)	45%	67%	27%
Trunk	10%	11%	9%
Abdominal/stomach	20%	11%	27%
Face/tongue	15%	11%	18%
Throat	5%	--	9%
Other	5%	--	9%



% yes	
On-Demand Treatment (n=9)	22%
Long-Term Prophylaxis (n=11)	27%

- One in five patients reported that their last untreated attack affected their face/tongue (15%) or throat (5%)
- Five attacks (25%) spread to other locations, including 1 to the larynx and 1 to the face

Figure 5. HAE-related Quality of Life During Untreated Attacks: Physical Health Impact



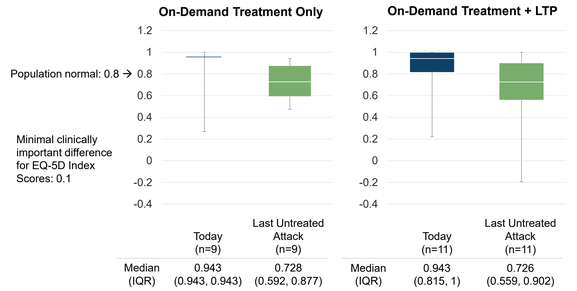
Treatment type	Rated top 2 (medium or a lot/severe)	Your Energy Level	Your Sleep	Your Activity Level
	On-Demand Treatment Only (n=9)	33%	33%	33%
	On-Demand Treatment + LTP (n=11)	36%	9%	36%

- At least 50% of participants reported that their last untreated attack impacted their energy levels, sleep, or activity levels at least "a little"

Figure 6. HAE-related Quality of Life During Untreated Attacks: Social Health Impact

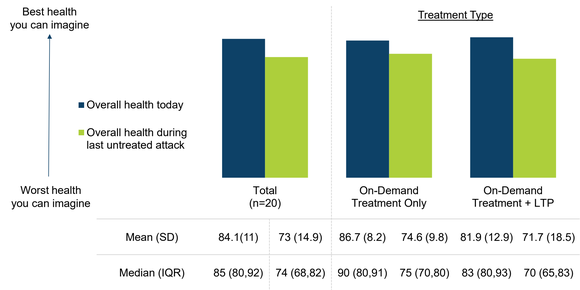
	Bottom 2	1	2	3	4	5	Top 2	Top 2 Treatment Type: On-Demand Treatment Only (n=9)	On-Demand Treatment + LTP (n=11)
	Strongly Disagree						Strongly Agree		
I felt embarrassed during my last HAE attack	50%	30%	20%		45%	5%	50%	33%	64%
My HAE attack made me feel socially isolated	55%	40%	15%	15%	25%	5%	30%	22%	36%
I felt like a burden to the people around me because I needed help during the attack	60%	50%	10%	15%	15%	10%	25%	33%	18%
My HAE attack caused strain with my family	65%	55%	10%	10%	20%	5%	25%	22%	27%
My HAE attack caused strain with my colleagues or coworkers	60%	60%		30%		10%	10%	0%	18%

Figure 7. Physical and Mental Quality of Life (EQ-5D Index Scores) Today and During the Last Untreated Attack by Treatment



- QOL index scores decrease as attack severity increased from mild (median 0.736) to moderate (median 0.622)

Figure 8. EQ-5D-5L VAS (General Health) Scores for Current and Last Treated Attack



	Total (n=20)		On-Demand Treatment Only		On-Demand Treatment + LTP	
Mean (SD)	84.1(11)	73 (14.9)	86.7 (8.2)	74.6 (9.8)	81.9 (12.9)	71.7 (18.5)
Median (IQR)	85 (80,92)	74 (68,82)	90 (80,91)	75 (70,80)	83 (80,93)	70 (65,83)

- General health scores were worse at the time of attack for both treatment groups

Conclusions

- HAE patients receiving on-demand only and those also taking LTP reported that untreated attacks:
  - Often progressed in severity
  - Migrated to other locations, including the larynx
  - Were associated with negative impact on both social and physical health
- Decreased QOL and general health scores were reported during the untreated attacks
- Results emphasize the need for greater education on the implications of not treating HAE attacks and support guidelines that all attacks should be considered for treatment

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