

Anxiety Associated with On-demand Treatment for Hereditary Angioedema (HAE) Attacks

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Abstract

- Rationale:** All approved on-demand treatments for hereditary angioedema (HAE) attacks require parenteral administration. Parenteral therapies can be challenging to administer, resulting in anxiety and increased treatment burden. The current study aimed to characterize anxiety related to use of parenteral on-demand therapy for HAE attacks.
- Methods:** People with Type 1 or 2 HAE were recruited by the US Hereditary Angioedema Association to complete a 20-minute, self-reported, online survey between April and June 2023. Participants ≥ 12 years old, with ≥ 1 HAE treated attack with an approved on-demand therapy within the prior 3 months were included. Anxiety was rated on a scale of 0 "not anxious" to 10 "extremely anxious".
- Results:** Respondents included 80 adults and 14 adolescents with HAE (81% Type 1), 54% were receiving long-term prophylaxis (LTP) at the time of their last treated attack. Overall, 57% of respondents (adolescents: 71%; adults: 46%) reported feeling moderately to extremely anxious (4-10 on anxiety scale) about treating their last attack with on-demand treatment. Time to treatment correlated with increased anxiety. Respondents who were extremely anxious were 1.7 times more likely to treat ≥ 5 hours vs < 2 hours compared to those who were not/mildly anxious (95% CI: 0.55-5.44; unadjusted odds ratio). The top-ranked reasons for anxiety were related to route of administration or injection side-effects (e.g., pain/burning with injection or finding a vein to start infusion).
- Conclusions:** Data suggest adults and adolescents with HAE experience moderate/extreme anxiety when anticipating use of parenteral on-demand treatment. Results highlight the impact of treatment-associated anxiety on treatment delays. Effective alternatives to current parenteral on-demand treatments are needed to address treatment-related anxiety as a potential barrier to timely treatment.

Background

- 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 both the severity and duration of each attack¹⁻³
- All currently approved on-demand treatment options require parenteral administration, which can be challenging to administer and is, thereby, associated with treatment burden
- The current study aimed to characterize anxiety related to the acute use of parenteral on-demand therapy for HAE attacks

Methods

- The US Hereditary Angioedema Association recruited participants with Type 1 or 2 HAE between April and June 2023
 - Recruitment was stratified to include 50% of participants taking on-demand only and 50% receiving LTP plus on-demand
- Participants completed a 20-minute, self-reported, online survey that asked about their last treated HAE attack
- Participants were ≥ 12 years old and had to have treated ≥ 1 HAE attack within the prior 3 months using an approved on-demand therapy
- Anxiety was rated on a scale of 0 "not anxious" to 10 "extremely anxious"

Results

Table 1. Participant Demographics

	Total (N=94)	On-demand Only Treatment (46% n=43)	On-demand Treatment + LTP (54% n=51)	Adults (85% n=80)	Adolescents (15% n=14)
Current Mean Age, (SD)	39.4 (17.4)	42.6 (18.7)	36.7 (15.8)	43.8 (15.0)	14.4 (1.5)
Mean Age of Diagnosis, Years (SD)	18 (12.6)	19 (12.7)	17 (12.5)	20 (12.5)	6 (4.1)
Gender					
Male	28%	23%	31%	21%	64%
Female	72%	77%	69%	79%	36%
Race/Ethnicity					
White	87%	91%	84%	89%	79%
Hispanic or Latino	9%	2%	14%	8%	14%
Black/African American	3%	2%	4%	3%	7%
American Indian or Alaskan Native	2%	2%	2%	-	14%
Asian	3%	5%	2%	4%	-
Other	1%	-	2%	1%	-
HAE Type					
Type 1	81%	79%	82%	81%	79%
Type 2	19%	21%	18%	19%	21%

- Respondents included 80 adults and 14 adolescents with an average age of 39 years (Table 1)
- The sample was predominately female (72%) and White (87%)
- At the time of their most recent treated attack, 54% of participants were on prophylaxis, and 46% were using on-demand treatment only
- Most participants (81%) reported having Type 1 HAE

Figure 1. On-demand Therapy Used for Last Treated Attack

On-demand Therapy	On-demand Only Treatment (n=43)	On-demand Treatment + LTP (n=51)	Adults (n=80)	Adolescents (n=14)
Icatibant	65%	63%	66%	NA*
Recombinant C1 Esterase Inhibitor	18%	21%	13%	50%
Plasma Derived C1 Esterase Inhibitor	15%	14%	9%	50%
Ecaltantide	2%	2%	3%	0%

*Not approved for patients under 18 years old.

- The initial on-demand treatment was typically icatibant (branded and generic) for adults and recombinant C1 esterase inhibitor or plasma derived C1 esterase inhibitor for adolescents (Figure 1)

Disclosures

In relation to this presentation, the authors declare the following, real or perceived conflicts of interest:

- Receipt of grants/research support: No conflicts of interest
- Receipt of honoraria or consultation fees: Cristine Radojicic: KalVista Pharmaceuticals, BioCryst, CSL Behring, Austria, Julie Ulloa and Sherry Danese: KalVista Pharmaceuticals, Sandra Christiansen: KalVista Pharmaceuticals, BioCryst, US HAEA Medical Advisory
- Participation in sponsored speaker bureau: Cristine Radojicic: CSL Behring
- Stock/shareholder: Vibha Desai and Paul Audhya: KalVista Pharmaceuticals
- Vibha Desai and Paul Audhya are employees of KalVista Pharmaceuticals

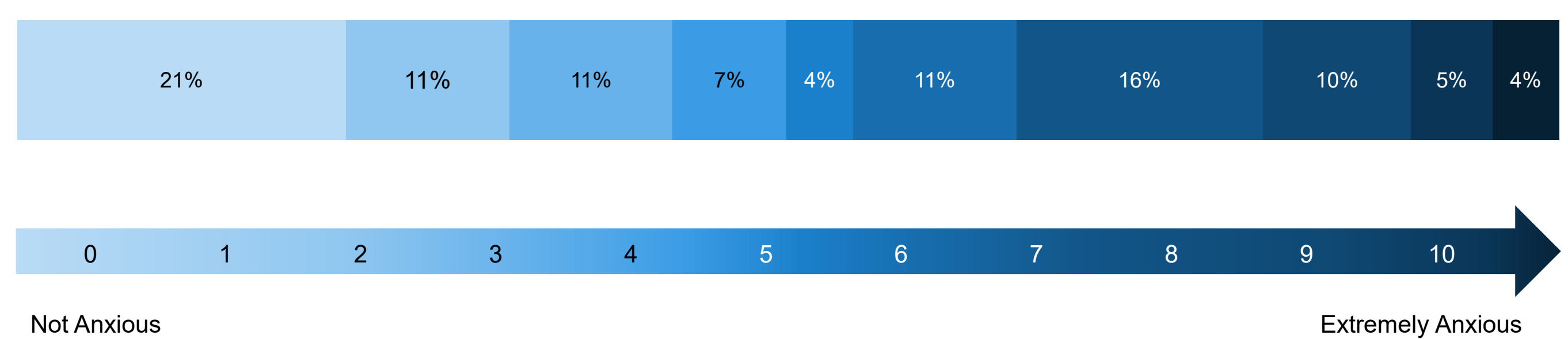
Results

Figure 2. Long-Term Prophylaxis at the Time of Last Treated Attack (n=51)

Long-Term Prophylaxis	% of Patients	Adults (n=43)	Adolescents (n=8)
Lanadelumab	57%	63%	25%
Subcutaneous Human C1 Esterase Inhibitor	24%	26%	13%
Berotrastat	14%	9%	38%
Intravenous Human C1 Esterase Inhibitor	6%	2%	25%

- Among those on long-term prophylaxis at the time of the last treated attack, lanadelumab was the most common treatment among adults, whereas adolescents were most often treated with berotrastat (Figure 2)

Figure 3. Anxiety about Treating with On-demand Treatment



- Mean (SD) anxiety was 4.0 (3.2)
- Overall, 57% reported feeling moderately (4-6 on the anxiety scale) to extremely anxious (7-10 on anxiety scale) about treating their last attack with on-demand treatment (Figure 3)

Figure 4. Patients Reporting Moderate to Extreme Anxiety

On-demand Treatment	On-demand Treatment + LTP	Percentage of Patients Reporting Moderate to Extreme Anxiety						
		Adults (n=80)	Adolescents (n=14*)	<1 hour (n=18*)	1 to <2 hours (n=15)	2 to <5 hours (n=37*)	5 hours to <8 hours (n=18*)	≥ 8 hours (n=6*)
47%	53%	46%	71%	33%	53%	54%	56%	50%

- Patients using on-demand only (47%) and those using on-demand + LTP (53%) had similar levels of moderate to extreme anxiety (Figure 4)
- 71% of adolescents reported moderate to extreme anxiety, compared to 46% of adults
- 54% reported moderate to extreme anxiety when treating in ≥ 2 hours to < 5 hours, compared to 33% when treating within < 1 hour from the attack onset
 - Respondents who were extremely anxious were 1.7 times more likely to treat in ≥ 5 hours rather than in < 2 hours compared to those who were not/mildly anxious (95% CI: 0.55-5.44; unadjusted odds ratio)

Figure 5. Reasons for Anxiety Associated with On-demand Treatment (n=74)

Reasons for Anxiety	On-demand Only Treatment (n=35)	On-demand Treatment + LTP (n=39)	Ranked 1 st			
			Adults (n=62)	Adolescents (n=12*)	Subcutaneous On-demand Treatment (n=45)	Intravenous On-demand Treatment (n=29)
Anticipating burning or pain with the injection	12%	13%	13%	8%	18%	3%
Finding the vein to start the intravenous infusion	12%	13%	8%	33%	2%	28%
Desire not to "waste" an on-demand treatment if the attack was less severe than I thought	11%	5%	13%	-	16%	3%
Running out of on-demand treatment if I needed it later	10%	6%	11%	-	16%	-
Uncertainty about whether the treatment would work	8%	8%	7%	17%	4%	14%
Uncertainty about how long the treatment would take to begin working	8%	10%	10%	-	13%	-
The cost of the on-demand treatment	7%	3%	8%	-	7%	7%
Anticipating side effects from the injection	7%	3%	7%	8%	7%	7%
Finding someone to help me administer the treatment	7%	8%	7%	8%	2%	14%
Worry about a rebound attack after the first treatment	4%	5%	5%	-	4%	3%
The process of preparing my treatment	4%	5%	3%	8%	2%	7%
Finding a private area to administer the treatment	4%	5%	5%	-	2%	7%
Uncertainty if the attack would become severe enough to treat	3%	5%	2%	8%	2%	3%
The need to use a second dose for the same attack	3%	3%	2%	8%	2%	3%
I am afraid of needles	1%	3%	2%	-	2%	-

- The top reason for anxiety associated with treatment reported by on-demand only patients was a desire to not waste on-demand therapy if the attack was less severe (17%), while LTP patients reported pain/burning with injection (13%), finding a vein to start infusion (13%), and running out of on-demand therapy (13%) as their top concerns (Figure 5)
- The top concerns among adults were pain/burning with injection (13%) and a desire to not waste on-demand therapy (13%), while adolescent patients reported finding a vein to start infusion (33%) and uncertainty if the treatment would work (17%) as their top concerns

Conclusions

- Both adults and adolescents with HAE reported moderate to extreme anxiety when anticipating use of parenteral on-demand treatment, irrespective of use of on-demand treatment only or on-demand plus LTP
- The results of this study highlight the association between delayed treatment and treatment-related anxiety, with a higher proportion of patients who delayed treatment experiencing moderate to extreme anxiety
- Effective non-parenteral alternatives to current on-demand treatments may help to address treatment-related anxiety as a potential barrier to timely treatment

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