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Psychological Burden Associated with Injectable HAE On-demand Treatments: A Patient and Caregiver Interview Study

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Background

- Hereditary angioedema (HAE) is characterized by unpredictable, painful, and debilitating attacks of swelling of the skin and/or submucosa, and is potentially life-threatening if patients experience a laryngeal attack[1]
- Patients and caregivers report that emotional and logistical challenges with injectable on-demand medication led to delaying or not administering on-demand treatment for attacks[2-4]
- We present results from our qualitative study describing patient- and caregiver-reported psychological burden and primary causes of such impact associated with current injectable on-demand treatment

Methods

- Patients and caregivers of patients with HAE were recruited via the Hereditary Angioedema Association (US) and HAE International (UK)
- Eligibility
  - – Adolescents (aged 12–17 years) or adults (aged ≥18 years) with a self-confirmed HAE Type 1/2 diagnosis, ≥1 HAE attack in the past 6 months, and prior experience using on-demand treatments for HAE
  - – Patient-caregivers had the same requirements as adult patients, but also cared for an adult or child (aged ≤17 years) with HAE
    - Patient-caregiver data are included only in the “Patient” subgroup
  - – Caregivers (aged ≥18 years) were a primary caregiver for a patient (care-recipient) with HAE
- Semistructured, qualitative interviews were conducted using interview guides tailored to respective subgroups
  - – Questions were open-ended; data were analyzed using thematic analysis to identify key themes and subthemes
  - – Many adult patients rated their attack using a visual analog scale (VAS) (0 [no symptoms] to 100 [worst symptoms ever])

Results

Study participants

- Interview participants (N=25) were based in the UK and US (**Table 1**)
  - – Seventeen were patients (7 adults, 5 adolescents, and 5 patient-caregivers) and 8 were caregivers (4 of adults, 4 of children)

Table 1. Demographic and clinical characteristics

Demographic characteristic	Patients (n=17)	Caregivers (n=8)
Country of residence, n (%)		
US[a]	11 (65)	6 (75)
UK[b]	6 (35)	2 (25)
Age, y		
Mean (SD)	34 (16.1)	43 (7.2)
Range	12–60	33–52
Sex, n (%)		
Female	12 (71)	7 (88)
Race, n (%)		
White	13 (77)	7 (88)
Clinical characteristics of individual with HAE[c] *Patients and care-recipients*		
Time since last attack (days)		
Mean (SD)	35 (54.6)	71 (86.0)
Range	1–180	2–270
Location of last attack,[d] n (%)		
Abdomen	9 (53)	3 (38)
Extremities/limbs	5 (29)	4 (50)
Face	2 (12)	2 (25)
Other	1 (6)	0 (0)
Severity of last attack, n (%)		
Mild	4 (24)	2 (25)
Moderate	7 (41)	4 (50)
Severe	6 (35)	2 (25)
Attacks in last year		
Mean (SD)	8 (7.0)	7 (6.2)
Range	1–20	1–20
Time since diagnosis, years		
Mean (SD)	21 (15.2)	10 (9.4)
Range	3–47	5–31
LTP use, n (%)	14 (82)	6 (75)
Lanadelumab-flyo[e]	5 (28)	3 (38)
C1INH SC [human][f]	3 (18)	2 (25)
Berotralstat[g]	3 (18)	0 (0)
Other	3 (18)	1 (12)
None reported	3 (18)	2 (25)

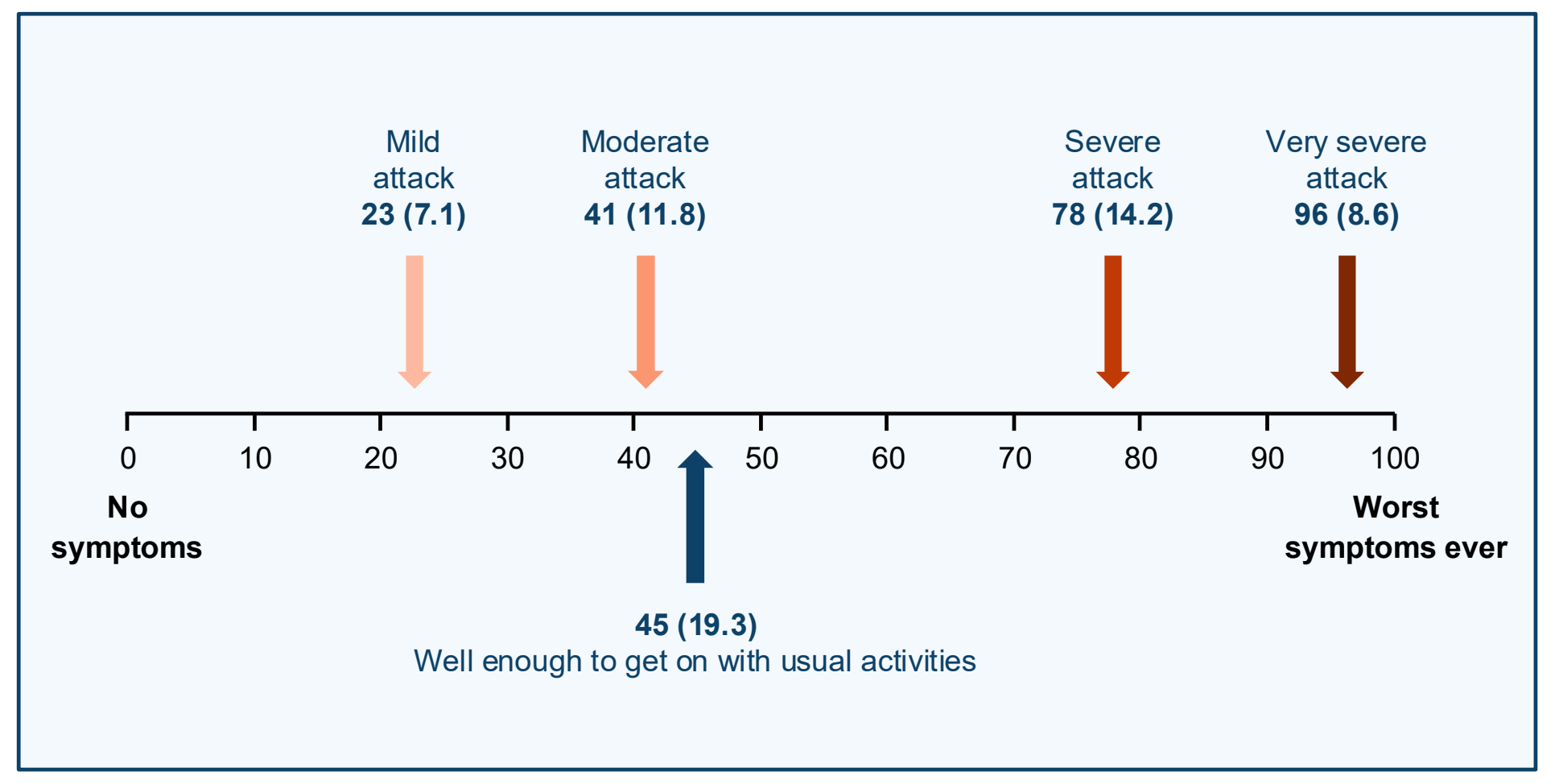
[a]Seventeen participants from the US comprised 3 adult patients, 4 patient-caregivers, 4 adolescent patients, 3 caregivers of adult patients, and 3 caregivers of adolescent patients. [b]Eight participants from the UK comprised 4 adult patients and 1 each from the other 4 subgroups. [c]Clinical data are self-reported for adult patient, patient-caregiver, and adolescent patient participants. Clinical data are proxy-reported for their care-recipient for participants who are caregivers of adults or children. [d]Cumulative percentages do not equal 100 because categories were not mutually exclusive. [e]Takhzyro. [f]Haegarda. [g]Orladeyo.
C1INH: C1 esterase inhibitor; HAE: hereditary angioedema; LTP: long-term prophylactic; SC: subcutaneous.

Results

VAS ratings after last attack

- Patients reported feeling well enough to perform activities of daily living when they had a mean VAS rating of 45, just above the mean rating of 41 for moderate attacks (**Figure 1**)

Figure 1. Qualitative VAS rating-task results among adult patients (n=7), mean (SD).



[a]One respondent confirmed that they were currently experiencing an attack at the time of interview, giving a rating of 75. All other participants rated their current symptoms as “0.”
VAS: visual analog scale.

Use of approved on-demand treatment

- In all, 11 patients and 3 caregivers reported use of icatibant (subcutaneous [SC] administration) and 6 patients and 5 caregivers reported use of a C1 esterase inhibitor (C1INH; intravenous [IV] administration) as their primary on-demand treatment (**Table 2**)
  - – Nearly 64% reported that C1INH was administered by a health care professional
  - – No adolescents self-administered their injectable on-demand treatment
- Although a number of participants (n=10/25; 40%) associated increased severity and duration of attacks with treatment delays, all reported delaying injectable on-demand treatment at least once in the past (**Table 2**)

> **“Where you’ve delayed taking treatment then it’s a bit worse than it would have been if you’d taken it an hour before.”**
> *Adult with HAE (UK)*

- Most (n=20/25 participants, 80%) reported foregoing treatment for some attacks (**Table 2**)

> **“We live in a very hot area and it gets up into the hundreds, so we don’t like keeping it in the car even in the cooler. Um, so we just make sure to come home if we’re experiencing anything, and that can cause a delay and it cause[s] the swelling to get worse and it can be uncomfortable for them.”** *Caregiver to adult with HAE (US)*
>
> **“I did not like it, it was very, very painful and it hurt a lot. So after that, there was moments like with my foot or something, where I would be like, ‘I’ll just hop around a lot’ instead of taking the shot because of just how bad it was.”** *Adolescent with HAE (US)*

Table 2. Typical on-demand treatment use

Characteristic of use, n	Icatibant (SC)	C1INH (IV)[a]
Primary treatment	14	11
Patients	11	6
Caregivers	3	5
Administration		
Self	8	4[b]
Adults[c]	8	4
Adolescents[d]	0	0
Caregiver/family member	6	1[b]
Health care professional	0	7
Frequency of use		
Treats every attack/suspected attack	4	1
Does not treat every attack	10	10
Location of administration		
Home only	9	1
Home or away from home	2	2
Hospital/medical facility	0	7
Not described	3	1

Counts include unprompted and prompted mentions. Counts include self-reported responses by patient participants and proxy-reported responses by caregiver-participants and could, therefore, have resulted in double counting of reports from patients and caregivers related to each other.
[a]On-demand plasma-derived C1INH for all participants except 1 adult and 1 adolescent respondent who had been prescribed recombinant C1INH. [b]Combination of self-administration and administration by spouse. [c]N=10. [d]N=4.
C1INH: C1 esterase inhibitor; IV: intravenous; SC: subcutaneous.

- Patients (n=6) and caregivers (n=6) reported feelings of anxiety and worry related to preparing and administering treatments quickly and correctly
  - – This anxiety was more pronounced in patients self-administering IV treatments, as the preparation and administration took longer and was more complex

> **“I’m a little bit shaky and a little bit nervous when I’m doing it.”** *Adult with HAE (UK)*
>
> **“It does trigger off his anxiety, which makes it harder for me to get him treatment, for him to even want to go get treatment to the hospital, any medicines out of fear of injections.”** *Caregiver to child with HAE (US)*
>
> **“I’m a nervous wreck, praying that it works and it works fast.”** *Caregiver to adult with HAE (US)*

- Additionally, 4 patients described their fear of treatment, often related to the use of needles

> **“Since it [needle] was this big I feel like I would have been panicking a lot because I don’t like needles.”**
> *Adolescent with HAE (US)*

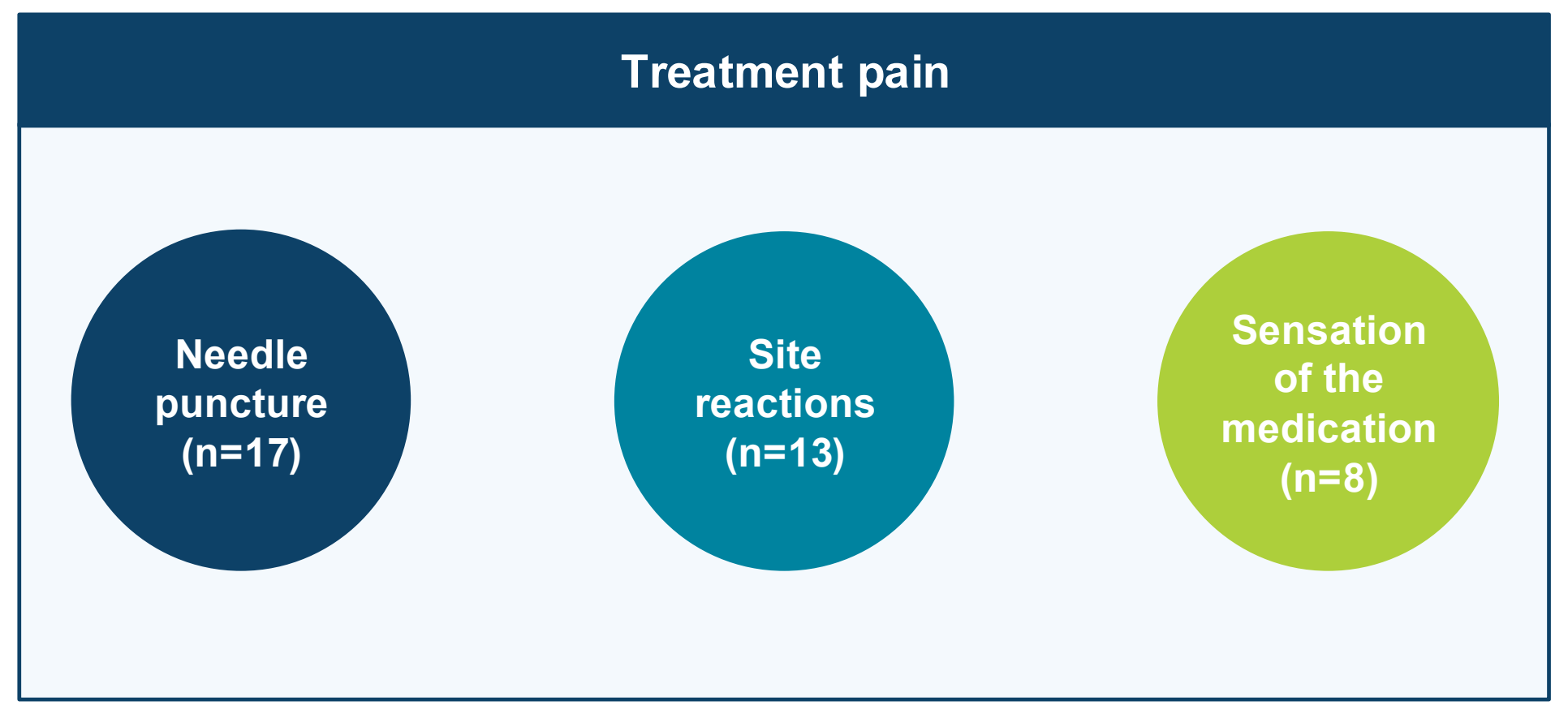
  - – Some caregivers (n=4) also reported stress of not only learning how to inject the treatments, but also knowing they were causing pain to their loved one

> **“I’d never injected anyone before and so that was nerve-racking.”** *Caregiver to adult with HAE (US)*
>
> **“Sometimes my husband would get really angry with me because some injections were less painful, some injections were really, really painful so he would say—.”**
> *Caregiver to adult with HAE (US)*

- Most respondents described pain and discomfort with injectable treatments as a primary source of psychological distress related to their injectable on-demand treatments (**Figure 2**)
  - – Painful administration (n=19) was among the most commonly reported concerns
  - – Patients described the feeling of icatibant entering the body as painful/burning, whereas C1INH was described as a discomfort/coldness
    - The sensation of icatibant or C1INH was described as worse than the actual injection, which resulted in hesitancy to treat…

> **“All I can say is it’s excruciating pain.”**
> *Patient-caregiver (US)*
>
> **“The first 24 hours after I inject it, it’s bumpy, and like I can feel it, and it’s sore…sometimes it actually hurts there worse than the initial attack was.”** *Adult with HAE (US)*

Figure 2. Sources of pain related to injectable on-demand treatment[a]



Treatment pain

Needle puncture (n=17)

Site reactions (n=13)

Sensation of the medication (n=8)

[a]Counts include unprompted and prompted mentions. Counts include self-reported responses by patient participants and proxy-reported responses by caregiver-participants, which could have resulted in the double counting of patients and caregivers related to each other.

- Logistical challenges with injectable on-demand treatments also contributed to increased anxiety and stress
  - – Nine patients and 5 caregivers discussed the lack of portability of treatments. Most participants described only carrying on-demand treatments when going on longer trips owing to challenges such as temperature control

> **“You have to be always conscious of the temperature outside, whether it’s hot, warm, too cold, you know?”**
> *Caregiver to an adult with HAE (US)*

  - – Seven patients described having to leave work or school to administer their treatments. This was due to not having access to treatment in these locations, not feeling comfortable, or needing to recover from the administration

> **“One of the hardest parts is when we don’t have it with us, and we have to like rush home to make sure we have it to give it to him."** *Caregiver to adult with HAE (US)*
>
> **“A lot of it is also 'cause my mom works, and so I don’t always have her immediately there to come give me the shot, I have to usually wait until it’s like… a better time or if her boss is willing to let her off early or just until she is out of work and can get home.”** *Adolescent with HAE (US)*

Perceptions of oral treatment

- All participants expressed interest in an oral on-demand treatment when asked directly, with some suggesting this spontaneously during interviews
- Several participants (n=8) indicated that if they had oral on-demand treatment available, they would treat attacks sooner

> **“With a pill, you wouldn't have to go to the hospital, that you could have it at home, it wouldn't need to be refrigerated; it is something easy to take.”** *Caregiver to a child (US)*

- Over half of participants reported positive perceptions of a potential oral therapy, including dosing flexibility, no preparation, fast and discrete administration, no storage requirements, and increased portability

> **“The more portable it is, it might be an option to take it to work with me or something like that or, if it’s easy to do, obviously uh, if something happens at work or right before work, I can do it in a timely manner and not have to miss out on missing work.”** *Adult with HAE (US)*

- Most patients and caregivers stated that they would prefer oral treatments because they could avoid the pain and emotional effects of injecting treatments
  - – Most participants considered swallowing a tablet easier and quicker than injecting treatment, thus potentially helping to avoid attack progression and reduce duration

> **“I wouldn’t have to talk myself into treating it, I would just be able to treat it immediately and probably not have to lose out on work or anything if it’s immediately treated and starting to already get better as the attack starts.”** *Adult with HAE (US)*

Conclusions

- **All participants reported delaying or foregoing on-demand injectable treatment of attacks at least once**
- **All patients and caregivers described negative effects on health-related quality of life related to their use of injectable on-demand therapy, often citing pain of injections and logistical barriers to administration**
- **An oral on-demand option may help address reported and perceived barriers to treatment**

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