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Anxiety Associated With Parenteral On-Demand Treatment for Hereditary Angioedema Attacks in Patients From Italy

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Background

- Currently, all approved on-demand treatments (ODs) for managing hereditary angioedema (HAE) attacks require parenteral (intravenous [IV] or subcutaneous [SC]) administration
  - Several ODs are approved in Italy, specifically IV plasma-derived and recombinant C1 inhibitors (C1INH) and SC icatibant
- Patients with HAE often experience anxiety due to the unpredictable, and debilitating nature of attacks,[1] as well as anxiety surrounding the administration of injectable OD, which is associated with pain and injection-site reactions[2]
- Despite guidelines recommending the early treatment of all attacks, many patients with HAE elect to not treat their attacks or to delay treatment[1–5]
- Compared with those who treat early, a higher proportion of patients who delay treatment report feeling "moderately" to "extremely" anxious[1,6]
- This study aimed to further characterize the extent of anxiety associated with the use of parenteral OD in an Italian population

Methods

- Individuals with HAE Type 1 or Type 2 were recruited between September 2023 and January 2024 through the Italian Network for Hereditary and Acquired Angioedema (ITACA)—which comprises 26 reference centers for angioedema—to complete an online survey
- Eligible participants were aged ≥12 years who had ≥1 attack treated with an approved OD in the previous 3 months
  - Adult patients and parents of adolescents provided informed consent; adolescents provided informed assent
- Data entered into the ITACA registry were confirmed by reference center physicians
- Participants were asked to rate their anxiety about using OD during their last attack on a scale of 0 ("not anxious") to 10 ("extremely anxious")
  - All outcomes were summarized using descriptive statistics

Results

Table 1. Demographic and clinical characteristics

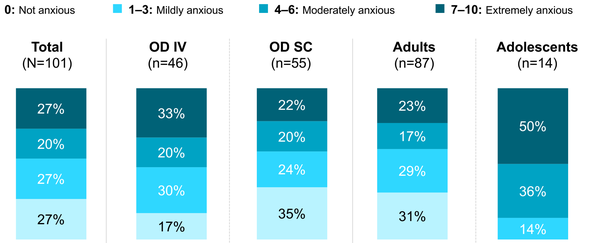
	Overall (N=101)	OD IV (n=46)	OD SC (n=55)	Adults (n=87)	Adolescents (n=14)
Current age, mean (SD), year	38 (16.2)	35 (16.8)	41 (15.3)	42 (14.0)	15 (1.6)
Age group (years)					
Adults (≥18)	87 (86)	36 (78)	51 (93)	87 (100)	N/A
Adolescents (12 to <18)	14 (14)	10 (21.7)	4 (7.3)	N/A	14 (100)
Age at diagnosis, mean (SD), year	17 (14.7)	14 (15.2)	19 (14.0)	18 (15.2)	7 (3.1)
Female	61 (60)	32 (70)	29 (53)	54 (62)	7 (50)
HAE type					
Type 1	94 (93)	43 (93)	51(93)	81 (93)	13 (93)
Type 2	7 (7)	3 (7)	4 (7)	6 (7)	1 (7)
Comorbidities					
Anxiety	15 (15)	7 (15)	8 (14.5)	13 (15)	2 (14)
Thyroid disease	10 (10)	6 (13)	4 (7)	10 (11)	0
Anemia	7 (7)	5 (11)	2 (4)	7 (8)	0
Hypertension	7 (7)	2 (4)	5 (9)	7 (8)	0
Autoimmune disorder	5 (5)	3 (6.5)	2 (4)	5 (6)	0
Liver disease	5 (5)	1 (2)	4 (7)	4 (5)	1 (7)
OD used					
Icatibant	55 (54)	0	55 (100)	51 (59)	4 (29)
Plasma-derived C1INH	46 (46)	46 (100)	0	36 (41)	10 (71)

Values shown are *n* (%) unless otherwise noted. C1INH, C1 inhibitor; HAE, hereditary angioedema; IV, intravenous; N/A, not applicable; OD, on-demand treatment; SC, subcutaneous.

Respondents

- Fifteen respondents (15% [15/101]) were diagnosed with an anxiety disorder by a physician (females 15% [9/61]; males 15% [6/40]; adults 15% [13/87]; adolescents 14% [2/14]) (**Table 1**)

Figure 1. Anxiety about treating with OD

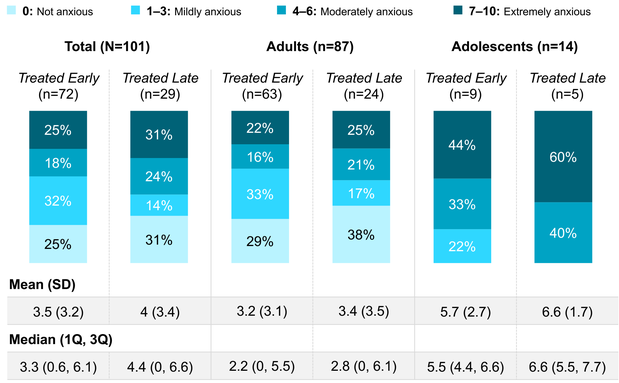


	Total (N=101)	OD IV (n=46)	OD SC (n=55)	Adults (n=87)	Adolescents (n=14)
Mean (SD)	3.7 (3.2)	4.2 (3.2)	3.3 (3.2)	3.3 (3.2)	6.1 (2.4)
Median (1Q, 3Q)	3.3 (0.0, 6.6)	4.4 (1.1, 6.6)	2.2 (0.0, 5.5)	2.2 (0.0, 5.5)	6.1 (4.4, 7.7)

OD, on-demand treatment.

- Approximately one-third (27%) of all respondents and 50% of adolescents reported feeling "extremely" anxious about treating their last attack with OD (**Figure 1**)
  - A total of 47% of all respondents (47/101), 86% of adolescents (12/14), and 80% of respondents diagnosed with comorbid anxiety (12/15) felt "moderately" (anxiety level rating: 4–6) or "extremely" anxious (anxiety level rating: 7–10) about treating their last attack with OD
  - A higher percentage of respondents taking IV OD (n=46) versus SC OD (n=55) felt "extremely" anxious (33% vs 22%, respectively)

Figure 2. Association between delayed injectable OD and treatment-related anxiety

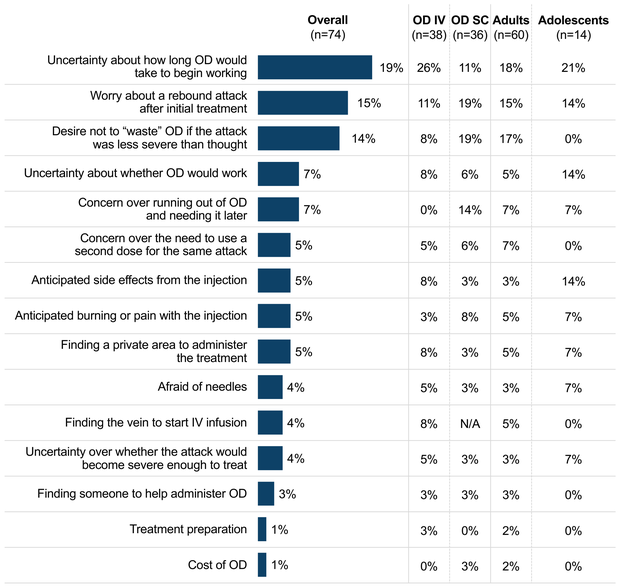


	Total (N=101)		Adults (n=87)		Adolescents (n=14)	
	Treated Early (n=72)	Treated Late (n=29)	Treated Early (n=63)	Treated Late (n=24)	Treated Early (n=9)	Treated Late (n=5)
Mean (SD)	3.5 (3.2)	4 (3.4)	3.2 (3.1)	3.4 (3.5)	5.7 (2.7)	6.6 (1.7)
Median (1Q, 3Q)	3.3 (0.6, 6.1)	4.4 (0, 6.6)	2.2 (0, 5.5)	2.8 (0, 6.1)	5.5 (4.4, 6.6)	6.6 (5.5, 7.7)

OD, on-demand treatment.

- When asked whether they had treated their attack "early" or "late," 71% (72/101) of respondents reported treating their attack early (**Figure 2**)
  - The mean (SD) time to OD in these respondents was 2.1 (1.7) hours compared with 5.0 (3.4) hours for those who treated late
- Compared with those who treated early, higher proportions of both adults and adolescents who did not treat early reported "moderate" to "extreme" anxiety (**Figure 2**)

Figure 3. Top-ranked reasons for anxiety among those who felt anxious, n=74



IV, intravenous; OD, on-demand treatment.

- Among the 74 respondents (73%) who reported feeling anxious, the top-ranked reasons for anxiety are shown in **Figure 3**
  - The most common reasons for anxiety were uncertainty about how long treatment would start working (19%), worry about a rebound attack (15%), and desire not to waste OD (14%)
  - The most common administration-related reasons for anxiety were side effects from injection, finding a private area to administer, and finding a vein to start infusion among those receiving IV on-demand treatment (8%); and anticipating burning or pain with injection among respondents using SC treatment (8%)

Conclusions

- **A substantial proportion of survey respondents experienced "moderate" to "extreme" anxiety about using parenteral OD, including most adolescents and most individuals diagnosed with an anxiety disorder**
- **Data showed an association between delayed OD and treatment-related anxiety, with a higher proportion of patients who did not treat early reporting "moderate" to "extreme" anxiety**
  - **These observations are consistent with data from a US population[4]**
- **The most common administration-related reasons for anxiety among respondents receiving injectable on-demand treatment were side effects from injection, finding a private area to administer treatment, finding a vein to start infusion (IV), and anticipating burning or pain with injection (SC)**

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