

SUPPLEMENTARY MATERIAL

Table 1. Demographic and clinical characteristics of the sample (n = 88)

Characteristics	
Age (mean \pm SD), (range) (y)	44.6 \pm 14.9, (18-75)
Gender, n (%)	
Female, Male	49 (55.7); 39 (44.3)
HAE-C1INH, type I, (N, %)	87 (98.9)
HAE-C1INH, type II, (N, %)	1 (1.1)
Family history of death by asphyxiation. N, (%)	21/88 (23.9)
Age at onset of symptoms, mean \pm SD (range) (y)	15.0 \pm 10.7 (1.0-57.0)
Age at diagnosis, mean \pm SD (range) (y)	22.8 \pm 15.7 (1.0-68.0)
Diagnosis delay, mean \pm SD (range) (y)	15.8 \pm 34.1 (-94.0-117.0)
Nr. of angioedema attacks in the last 6 months	
Mean \pm SD, range	6.1 \pm 6.7 (0-33)
Median (Q1-Q3)	4.0 (1-10)
Complement levels at diagnosis	
C4, (N), mean \pm SD (range) (mg/dL)	79/88, 7.78 \pm 4.27 (1.56-19.30)
C1INHf (N), mean \pm SD (min-max) (%)	37/88, 20.81 \pm 9.55 (4.50-46.41)
C1INH, (N), median (IQR) (mg/dL)	72/88, 8.14 (5.60-11.15)
Complement levels (last 6 months)	
C4 (N, mean \pm SD, range) (mg/dL),	86/88, 6.96 \pm 3.31 (1.53-15.60)
C1INHf, (N, mean \pm SD, range) (%)	84/88, 21.32 \pm 10.22 (5.43-60.49)
C1INH (N, median, IQR) (mg/dL),	81/88, 6.98 (4.95 – 8.61)
Total number of angioedema attacks in the last 6 months (N, %), (mean \pm SD, range)	508 (100.0), 6.1 \pm 6.7 (0-33)
Peripheral (N, %), (mean \pm SD, range)	255 (50.2), 3.1 \pm 4.4, (0-18)
Abdominal (N, %), (mean \pm SD, range)	148 (29.1), 1.8 \pm 2.7 (0-12)
Multiple (N, %), (mean \pm SD, range)	66 (13.0), 0.8 \pm 1.8, (0-11)
Genital (N, %), (mean \pm SD, range)	22 (4.3), 0.3 \pm 0.8, (0-6)
Facial (N, %), (mean \pm SD, range)	10 (2.0), 0.1 \pm 0.4, (0-2)
Upper airway (N, %), (mean \pm SD, range)	7 (1.4), 0.1 \pm 0.4, (0-2)
HAE-AS (N), mean \pm SD, range	84/88, 10.2 \pm 3.5, (1.0 – 15.6)
HAE-QoL (N), mean \pm SD, (range)	84/88, 100.8 \pm 23.9, (32.0 - 134.0)
Drug used for LTP (N, %)	29/88 (33.0)
Attenuated androgens (N, %)	18 (21.6)
Antifibrinolytics (N, %)	7 (8.0)
IV pdC1INH (N, %)	4 (4.5)

Abbreviations: C1INH: C1INH protein, C1INHf: C1 inhibitor functional activity. Normal range C4: 14-60 mg/dL, C1INH: 16-33mg/dL, C1INHf: >50%. IV, intravenous; LTP, Long term prophylaxis; pdC1INH, human plasma derived C1 esterase inhibitor concentrate; SC, subcutaneous; SD: standard deviation; y, year.

Table 2. Disease activity measured by HAE-AS in patients taking the different types of long-term prophylaxis.

	Long term prophylaxis				p
	On-demand treatment	Attenuated androgens	Antifibrinolytics	pdC1INH	
HAE-AS (0-30 scale)					
N	57/59	17/18	6/7	4/4	0.061
Mean ± SD	9.69 ± 3.53	10.25 ± 3.74	11.52 ± 2.32	14.07 ± 1.79	

IV: intravenous; pdC1INH: plasma derived C1 inhibitor

Table 3. Complement levels according to long term prophylaxis.

	Long term prophylaxis in the last 6 months		
	No	Yes	p
C4 at diagnosis (mg/dL)			
N	20/59	14/29	0.589
Mean ± SD	7.59 ± 4.17	8.15 ± 4.52	
C1INHf at diagnosis (%)			
N	20/59	14/29	0.228
Mean ± SD	19.32 ± 8.12	23.27 ± 11.42	
C1INH at diagnosis (mg/dL)			
N	47/59	25/29	0.948
Median (IQR)	8.00 (5.90 – 11.00)	8.28 (4.81 – 11.30)	
C4 last 6 months (mg/dL)			
N	58/59	26/29	0.796
Mean ± SD	6.90 ± 3.05	7.09 ± 3.85	
C1INHf last 6 months (%)			
N	58/59	26/29	0.179
Mean ± SD	20.32 ± 9.55	23.57 ± 11.46	
C1INH last 6 months (mg/dL)			
N	55/59	26/29	0.376
Median (IQR)	6.8 (4.86-8.39)	7.78 (4.89-12.25)	

IQR: Interquartile range; C4; complement fraction 4; C1INH: C1 inhibitor; C1INHf: C1 inhibitor functional activity.

Normal range C4: 14-60 mg/dL, C1INH: 16-33mg/dL, C1INHf: >50%.

Table 4. Complement values in patients taking the different drugs for long-term prophylaxis.

	Long term prophylaxis (LTP)				p
	Exclusive on-demand treatment	Attenuated androgens	Antifibrinolytics	pdC1INH	
C4 at diagnosis (mg/dL) N Mean \pm SD	20/59 7.24 \pm 3.97	10/18 10.26 \pm 5.60	3/7 8.29 \pm 4.59	1/4 **	0.167
C1INHf at diagnosis (%) N Mean \pm SD	20/59 20.43 \pm 7.79	10/18 23.10 \pm 13.10	3/7 23.24 \pm 9.11	1/4 **	0.694
C1INH at diagnosis (mg/dL) N Median (Q1-Q3)	47/59 8.00 (5.90-11.0)	15/18 9.45 (6.40-11.80)	7/7 4.80 (4.43 – 11.20)	3/4 11.0 (4 - ***)	0.550
C4 last 6 months (mg/dL) N Mean \pm SD	58/59 6.89 \pm 3.05	16/18 5.75 \pm 2.99	6/7 7.57 \pm 4.44	4/4 9.85 \pm 4.00	0.270
C1INHf last 6 months (%) N Mean \pm SD	58/59 20.31 \pm 9.54	16/18 25.58 \pm 12.91	6/7 19.12 \pm 7.98	4/4 22.18 \pm 9.51	0.305
C1INH last 6 months (mg/dL) N Median (Q1-Q3)	55/59 6.80 (4.86-8.39)	16/18 7.30 (4.72-13.43)	6/7 6.96 (4.00-10.38)	4/4 10.26 (5.85-12.35)	0.565

LTP with pdC1INH was not taken into account because there was only one patient, C4 and C1INHf were considered as a constant for the comparison. * Undetermined.

C1INH: C1 inhibitor; C1INHf: C1 inhibitor functional activity; C4: complement fraction 4; LTP: long term prophylaxis; pdC1INH: plasma derived C1 inhibitor.