

Hereditary angioedema: Clinical presentation and socioeconomic cost of 200 French patients



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Clinical Implications

- Socioeconomic cost at the level of patient with hereditary angioedema is high. It is possible to effectively manage hereditary angioedema at much lower costs than previously reported with coordinated national management. This study promotes the development of home therapy and self-administration of specific treatment.

TO THE EDITOR:

Treatment options of patients with hereditary angioedema (HAE) are large and are codified in recent guidelines.¹ Use of health care system may be high. Two studies suggest that HAE may lead to substantial costs and burden, associated with attack severity.^{2,3} Lumry et al⁴ reported reasonably high health-related quality-of-life (HRQOL) scores for patients included in the Clinical Studies for Optimal Management of Preventing Angioedema with Low-Volume Subcutaneous C1-Inhibitor (C1-INH) Replacement Therapy trial. The objectives of the present study were to determine the costs (direct and indirect) and HRQOL associated with medical management of HAE in France.

We undertook an ancillary study of the SOS-HAE study,⁵ a multicenter cluster-randomized prospective trial that assessed morbidity (number of hospital admissions) after a telephone care-management used for patients with HAE. From March 2013 to June 2014, we prospectively enrolled patients older than 18 years with documented diagnosis of HAE. The complete method details can be found in the original article.⁵ We collected economic data and HRQOL based on the 3-level version of EuroQol five-dimensional questionnaire (EQ-5D-3L) in accordance with the Consolidated Health Economic Evaluation Reporting Standards statement.⁶ Resource utilization was prospectively collected during the 2 years of follow-up. The outcomes of interest were total direct medical costs, which included hospital admissions, drug use, emergency department (ED) visits, home nurse or physician visits, emergency service interventions, transportation covered by the French statutory health insurance, and consultations. We collected EQ-5D-3L self-administered questionnaires at baseline and at 6, 12, and 24 months. The utility values were based on French tariffs for the

corresponding scores. Missing data were replaced by values estimated by multiple imputation using hospitalization, ED admissions, and procedures as variables. The unit of analysis was the patient, data from the intervention and control groups were pooled, and a comparison between patients with long-term prophylaxis and without long-term prophylaxis was made.⁵

Information on health care resource utilization, productivity, and HRQOL was available for all 200 patients, who represented about 15% to 30% of all patients with HAE in France in 2014 (Table I). Four patients (2 in the control arm and 2 in the intervention arm) were lost after more than 4 months of follow-up (4, 14, 22, and 24 months, respectively). Two patients died at 12 and 14 months of follow-up (not related to HAE, due to breast cancer and leukemia). Missing data were less than 1% in both groups. One hundred sixty-four (82%) patients had HAE type I, 14 (7%) had HAE type II, and 22 (11%) patients had HAE with mutation of the gene encoding human coagulation factor XII. Nearly three-quarters (73%) of the study patients were receiving long-term prophylaxis (regular medication to reduce the burden of the disease by preventing/attenuating attacks in patients with confirmed HAE-1/2). No patients received long-term prophylactic plasma-derived C1-INH treatment. One hundred sixty-nine (85%) patients had experienced at least 1 attack during the follow-up. Among them, 105 (53%) had at least 1 severe event from an HAE attack. During 2 years, there were 2368 HAE attacks (mean of 12 attacks per patient), including 468 (20%) severe attacks. One hundred forty (70%) patients had at least an attack that involved the abdomen, 123 (62%) patients for limbs, 38 (19%) patients for lips, 31 (16%) patients for cheeks, 31 (16%) patients for larynx, 30 (15%) patients for genitals, 19 (10%) patients for eyelids, and 9 (5%) patients for tongue. On-demand medical treatment was required for 1706 (72%) attacks. Attacks were abdominal (1251 of 2368 [53%]), genital (141 of 2368 [6%]), peripheral (969 of 2368 [41%]), laryngeal (107 of 2368 [5%]), and facial (239 of 2368 [10%]) attacks. Treatments were tranexamic acid for 654 (28%) attacks, C1-INH concentrate for 186 (8%) attacks, and icatibant for 730 (31%) attacks. Self-administration was performed in 1429 (60%) attacks, whereas a home nurse administration was performed in 182 (8%) attacks. Emergency Medical Service interventions were required for 18 (1%) attacks, ED admissions for 53 (2%) attacks, intensive care unit admissions for 4 (0.2%) attacks, and hospitalization (in medical ward with a length greater than 24 hours) for 19 (1%) attacks.

A total of 199 (99.5%) patients had full 1-year data and 194 (97%) completed the 2-year follow-up. All costs are presented in Table II. The average yearly cost was €10,244 ± €17,365 (\$11,371 ± \$19,275) mostly driven by drug costs, which accounted for 97% of total medical costs. The average cost per attack was €775 ± €903 (\$860 ± \$1002). We compared patients with and without long-term prophylaxis, which included tranexamic acid, androgen, and progestin (Table II), and found a trend toward lower cost for the untreated patients who experienced fewer crises ($P = .08$). One hundred ninety-eight patients completed the questionnaires at 12 months and 194 at 24 months. The overall quality of life was rated excellent, very good, or good by 90% of the patient population, and 30% considered

TABLE I. Baseline characteristics of the study population

Characteristic of patients	N = 200
Demographic characteristics	
Female sex, n (%)	74 (37)
Age (y), median (Q1-Q3)	40 (29-54)
Coexisting conditions, n (%)	
Hypertension	20 (10)
Tobacco use	19 (10)
Diabetes	9 (5)
Dyslipidemia	18 (9)
Chronic heart failure	1 (0.5)
Chronic renal failure	1 (0.5)
Stroke	2 (1)
Cancer	10 (5)
Psychiatric disorders	0 (0)
Type of HAE, n (%)	
HAE type I	164 (82)
HAE type II	14 (7)
FXII-HAE	22 (11)
History of angioedema, n (%)	
Number of families included	153 (77)
Patients with at least 1 HAE sick parent	139 (70)
Patients with at least 1 children	132 (66)
Patients with at least 1 HAE sick children	119 (60)
Patients with at least 1 HAE sick sibling	96 (48)
Years since diagnosis, median (Q1-Q3)	14 (5-29)
Long-term and available emergency treatment at baseline, n (%)	
Androgen	63 (32)
Tranexamic acid	39 (20)
Progestin	41 (21)
Icatibant	149 (75)
C1-INH	53 (27)
Nurse-led formation on self-administration of specific therapy	185 (93)

FXII, HAE with mutation of the gene encoding human coagulation factor XII.

their health excellent. At 24 months, only 3 patients reported worsening of their health. Physical limitation for vigorous activities and work activities was limited in only 20%. Seven (4%) patients reported that physical health or emotional problems interfered with their normal social activities. Bodily pain and interference of pain with normal work and activities was present in 27 (14%) patients, and the same percentage reported getting sick a little easier than other people and not being as healthy as anybody they know. The EQ-5D scores converted into utilities at 12 months were 0.71 ± 0.12 and 0.70 ± 0.13 at 24 months. These figures did not differ between the patients with and without long-term prophylaxis.

This study suggests that HAE may lead to substantial direct and indirect costs, mainly driven by drug costs. In our study, long-term prophylaxis is probably a marker of severity because patients without long-term prophylaxis had fewer attacks. The total annual cost was €10,244 for an average patient with HAE, whereas in a US study,³ total annual costs per patient were estimated at \$42,000 (including indirect cost) or \$29,177 for direct costs only (rising with increasing attack severity) and were driven by ED visits and hospital stays as well as by higher

TABLE II. Health economics (resource use and costs) outcomes during the 2 years follow-up

Average cost $\pm$ SD per patient (€)	N = 200
Patients completed the 0- to 12-mo follow-up	
Drug cost	10,038 $\pm$ 10,334
ED visits + transportation	99 $\pm$ 25
Consultation GP/specialist	26 $\pm$ 10
Nurse	10 $\pm$ 2
Hospital cost	122 $\pm$ 176
Total average health care costs	10,296 $\pm$ 17,828
Average compensation for workdays lost	54 $\pm$ 89
Average total cost during the first year	10,350 $\pm$ 17,968
Patients completed the 12- to 24-mo follow-up	
Drug cost	10,287 $\pm$ 8,260
ED visits + transportation	101 $\pm$ 24
Consultation GP/specialist	27 $\pm$ 10
Nurse	10 $\pm$ 2
Hospital cost	118 $\pm$ 180
Total average health care costs	10,544 $\pm$ 17,525
Average compensation for workdays lost	55 $\pm$ 87
Average total cost during the second year for patients alive	10,599 $\pm$ 16,823
0-24 mo	
Average yearly total cost per patient	10,244 $\pm$ 17,365
Patients receiving long-term prophylaxis	
	N = 120
	12,019 $\pm$ 18,845
Patients without long-term prophylaxis	
	N = 80
	7,637 $\pm$ 14,668

GP, General practitioner.

€1 $\approx$ \$1.11 in 2015.

hospital costs in the United States. Another difference was a fewer rate of ED visits and hospitalizations in our study. Moreover, our patients were already integrated into an expert HAE network with therapeutic education programs. We hypothesize that this strategy of coordination combined with patient education reduced the economic burden.⁵

The quality of life reported by Lumry et al⁴ was higher than our results. Patients are included in a therapeutic trial in which prophylactic use of subcutaneous C1-INH twice weekly significantly reduced the frequency of acute attacks.⁷ In our study, no patient received prophylactic use of subcutaneous C1-INH.

HAE is a rare disease whose socioeconomic cost is high at the level of patient. It is possible to effectively manage HAE at much lower costs than previously reported with coordinated national management.

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