

Letter to the Editor

Home treatment of hereditary angioedema with icatibant administered by health care professionals

To the Editor:

Hereditary angioedema caused by C1-inhibitor deficiency (HAE-C1-INH) is a rare autosomal dominant disorder that manifests as recurrent unpredictable attacks of nonurticarial angioedema.¹ Attacks are typically localized to the skin or submucosal tissues, cause temporary disablement, and resolve within 48 to 96 hours.² Gastrointestinal edema can mimic an acute abdominal emergency, prompting unnecessary surgical exploration during attacks; critically, upper airway edema can potentially lead to suffocation.³ In addition to living with an unpredictable and potentially life-threatening disease, the need to attend hospital for acute treatment⁴ imposes further burdens on patients.

Development of home treatment strategies for patients with HAE-C1-INH is an important step toward improving the management of this debilitating condition. Studies of home-based⁴ and patient-administered⁵ C1-inhibitor concentrate have demonstrated the viability of acute treatment outside of clinical settings, and international guidelines advise that “home plasma-derived C1-inhibitor self-infusion programs should be offered to patients”³ and that “home therapy offers the possibility of earlier treatment and better symptom control, enabling patients to live more healthy, productive lives.”⁶

Icatibant, a subcutaneously administered selective bradykinin B₂ antagonist, was shown in 2 phase III randomized controlled trials to be effective and generally well tolerated for the symptomatic treatment of hereditary angioedema (HAE) attacks (types I and II) in adults. In these studies icatibant was administered by health care professionals (HCPs) in a clinical setting.⁷ We report our experience with icatibant home treatment administered by HCPs in a prospectively assessed, sizable patient sample. Adults with type I or II HAE (all types of attack) were eligible for inclusion. The study was approved by the institutional ethics board and conducted in accordance with the principles of Good Clinical Practice. All patients provided written informed consent.

Patients experiencing the onset of an attack were evaluated by an HCP at home (after a telephone consultation to establish the attack persistence). Attacks (any location and all severities) were treated by the HCP with a single 30-mg subcutaneous injection of icatibant (supplied in a prefilled 3-mL syringe) in the abdominal region, and attack characteristics and responses to treatment were assessed by patients. Nine patients were treated for 16 attacks: 10 attacks in 8 patients localized in the abdomen (one combined attack also involved the skin of abdomen), 3 attacks in 2 patients localized in the upper airway, and 3 attacks in 3 patients localized in the arm ($n = 2$) or foot ($n = 1$). One patient was treated for 4 attacks, 4 patients were treated for 2 attacks, and 4 patients were treated for a single attack.

Characteristics of both patients and attacks are summarized in Table I. Icatibant was administered within a median of 2.92 hours (range, 0.25–25.00 hours) after the attack’s onset. Median times to onset of symptom improvement were 0.83 hours (range, 0.25–0.85 hours) for cutaneous attacks, 0.50 hours (range, 0.42–1.00 hours) for upper airway attacks, and 0.57 hours (range, 0.25–3.25 hours) for abdominal attacks; times to complete resolution

of symptom were 10.00 hours (range, 6.50–19.50 hours), 6.08 hours (range, 4.00–6.75 hours), and 5.65 hours (range, 3.25–24.33 hours), respectively. Analysis of time between attack onset and icatibant administration (2-tailed Fisher exact test) showed no apparent effect on time to onset of symptom relief ($P = .24$) or time to complete resolution of symptoms ($P = .65$). Patients’ global assessment of attack severity demonstrated consistent improvements after icatibant administration (Table I). Repeated icatibant treatment in patients with multiple attacks (1 injection per attack) did not appear to affect efficacy. The severity of individual attack symptoms over time (symptom scores) are shown in Table E1 in this article’s Online Repository at www.jacionline.org. Patients also used a visual analog scale of attack severity (0 mm = absent and 100 mm = worst possible severity) to evaluate symptoms over time (see Fig E1 in this article’s Online Repository at www.jacionline.org).

HAE attack recurrence (emergence of new HAE symptoms in a different location within 48 hours) occurred in 2 patients. Patient 4 had an initial abdominal attack that completely resolved within 24 hours after administration of icatibant, but after 36 hours, cutaneous mild edema had developed in multiple locations; these symptoms resolved spontaneously within 24 hours without further treatment. Patient 5 had an initial cutaneous (arm) attack that completely resolved within 10 hours after icatibant treatment, but after 24 hours, moderate edema had developed in multiple locations (arm, leg, and torso, all occurring on the right side of the body), and she was treated with 500 IU of C1-inhibitor concentrate; symptoms resolved more slowly than usual, with complete resolution at 48 hours. All patients experienced injection-site reactions (including swelling, burning, itching, warm sensation, and pain) after icatibant administration; these were generally mild and resolved without intervention, usually within 4 to 6 hours. No drug-related systemic adverse events were reported.

These prospective data demonstrate for the first time that icatibant administered by HCPs at home has a similar efficacy and tolerability profile as icatibant administered in clinical settings. The onset of symptom relief after icatibant home treatment occurred within 0.25 and 3.25 hours, and all symptoms in all types of attack localization were completely resolved within 4.00 to 24.33 hours (4.00–6.75 hours for upper airway attacks). There was no apparent relationship between attack severity and response. Icatibant home treatment displayed a tolerability profile consistent with that reported in clinical studies.^{7,8} No drug-related systemic adverse events were reported. Mild, self-resolving injection-site reactions were reported by all patients, which is again consistent with the known tolerability profile of icatibant.^{7,8}

Attack recurrence was experienced in 2 cases (12.5% of evaluated attacks); this observation corresponds to phase III/IIIb clinical studies^{7,9} and to clinical experience that some HAE attacks require more than 1 dose of acute treatment. Only 1 recurrent episode required treatment (the HCP decided to administer 500 IU of C1-inhibitor concentrate). Complete resolution of symptoms after administration of C1-inhibitor concentrate occurred more slowly than usual, within 48 hours, suggesting that it might be necessary to supply 2 prefilled icatibant syringes for patients considering icatibant home treatment.

TABLE I. Patient and attack characteristics, responses to home-administered icatibant, and global assessments of attack severity (1 = absent, 5 = very severe) at baseline and 4 hours

Patient no., sex	Age at time of study (y)	Attack number: location	Time (h)			Global assessments	
			Attack onset to icatibant administration	Icatibant administration to symptom improvement	Icatibant administration to complete symptom resolution	Baseline	4 h
1, female	52	Attack 1: arm	2.00	0.25	6.50	3	1
		Attack 2: upper airway	3.08	0.42	6.08	2	1
		Attack 3: upper airway	0.25	1.00	6.75	3	2
		Attack 4: intra-abdominal	4.25	3.25	7.75	3	2
2, female	20	Attack 1: intra-abdominal	0.25	1.00	7.00	3	1
3, female	39	Attack 1: intra-abdominal	2.50	0.30	4.30	4	1
		Attack 2: upper airway	3.50	0.50	4.00	3	1
4, female	46	Attack 1: intra-abdominal/ abdominal skin	11.67	1.67	24.33	3	3
5, female	39	Attack 1: arm	1.30	0.83	10.00	4	2
6, female	31	Attack 1: intra-abdominal	1.83	0.50	3.25	3	1
		Attack 2: intra-abdominal	2.75	0.42	3.25	3	1
7, male	41	Attack 1: intra-abdominal	5.83	0.42	3.42	4	1
8, female	24	Attack 1: foot	10.08	0.85	19.50	5	2
		Attack 2: intra-abdominal	5.63	0.62	3.45	3	1
9, male	25	Attack 1: intra-abdominal	25.00	2.00	9.00	3	1
		Attack 2: intra-abdominal	0.50	0.25	24.00	3	1

Our findings suggest a role for icatibant home administration in helping patients with HAE-C1-INH in the management of their condition and provide support for the inclusion of icatibant in future recommendations for HAE-C1-INH home therapy.

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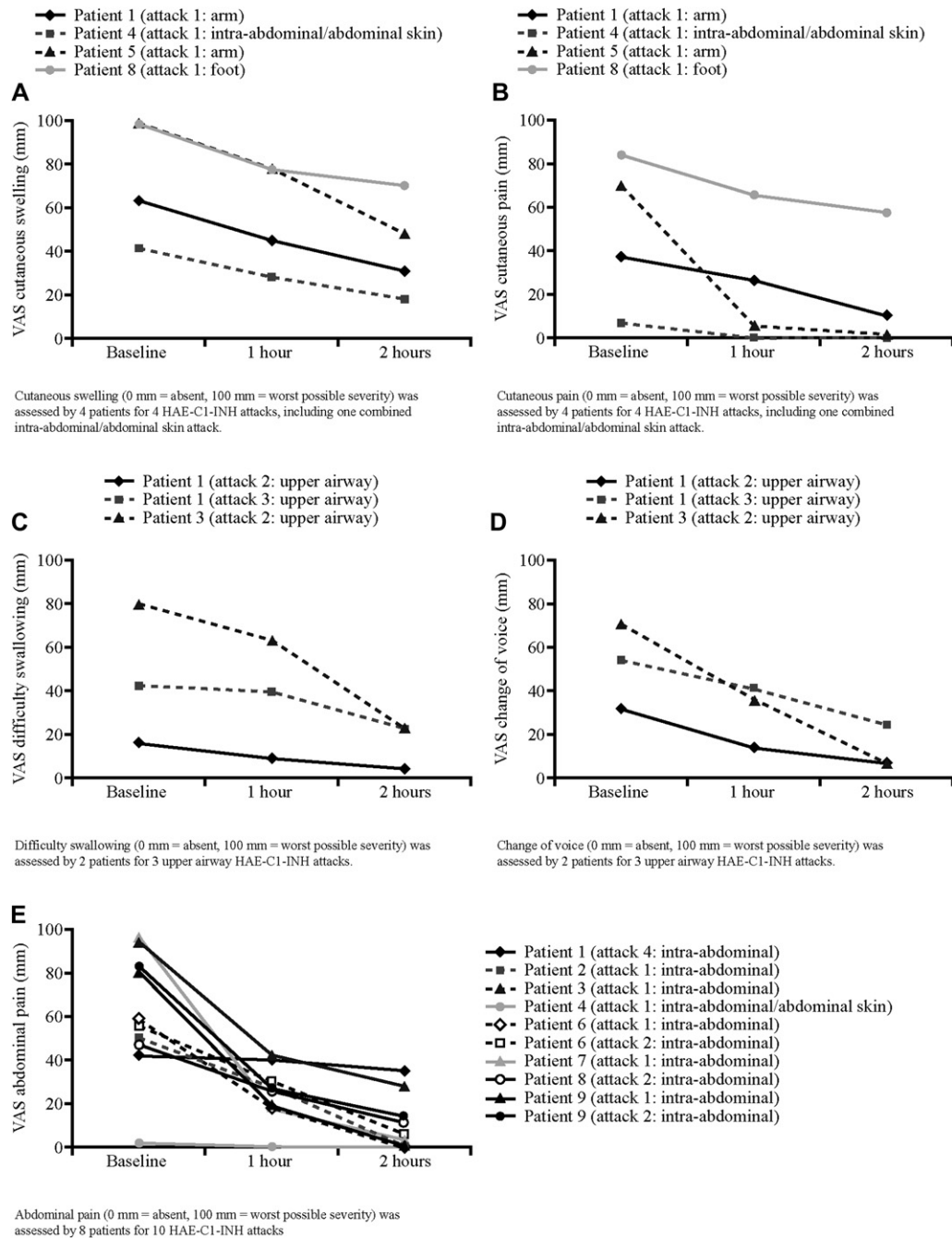


FIG E1. Patient-assessed visual analog scale (VAS) at baseline and 1 and 2 hours after icatibant home administration for cutaneous swelling (A), cutaneous pain (B), difficulty swallowing (C), change of voice (D), and abdominal pain (E).

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