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Federico Iuri

Prevalenza e gestione dell'Angioedema in Pronto Soccorso

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PREVALENZA E GESTIONE DELL' ANGIOEDEMA IN PRONTO SOCCORSO

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CODICE GIALLO

CODICE VERDE

CODICE ROSSO

3.2.4 Dispnea

CODICE	SINTOMO
	CARDIOPALMO
	COMPROMISSIONE RESPIRATORIA MODERATA
	DOLORE TORACICO IN ATTO
	SINCOPE / PRESINCOPE
	DISFONIA / MANIFESTAZIONI ALLERGICHE
	DIABETE MELLITO
	FATTORI DI RISCHIO PER EMBOLIA POLMONARE
	COMPROMISSIONE RESPIRATORIA MINORE
	TOSSE + FEBBRE
	TOSSE PROTRATTA / SINTOMI DI SOSPETTA TBC
	DISPNEA RIFERITA SENZA CRITERI DI PRIORITA'

3.2.11 Allergia

CODICE	SINTOMO
	DISPNEA
	SINCOPE / PRESINCOPE
	DISFONIA / DISFAGIA / ODINOFAGIA
	SINTOMATOLOGIA RAPIDAMENTE INGRAVESCENTE
	SINTOMATOLOGIA NON INGRAVESCENTE

2° LIVELLO

- TRAUMA
- DOLORE TORACICO
- SOSPETTA SEPSI E ALTERAZIONI TEMPERATURA
- DISPNEA
- CARDIOPALMO
- SINCOPE / PRESINCOPE
- CEFALEA
- DISTURBI NEUROLOGICI
- DISTURBI DEL COMPORTAMENTO
- DOLORE ADDOMINALE
- ALLERGIA
- EMORRAGIE NON TRAUMATICHE
- INTOSSICAZIONI
- GRAVIDANZA
- PROBLEMA SPECIFICO

1° LIVELLO

- COMPROMISSIONE DELLA COSCIENZA
- COMPROMISSIONE RESPIRATORIA
- COMPROMISSIONE EMODINAMICA
- SINTOMO PRIORITARIO
- GIUNTO CADAVERE

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SCOPO DELLA ANALISI

- Valutare la prevalenza di angioedema nei pazienti che si presentano in Pronto Soccorso.
- Valutare la capacità di riconoscimento di angioedema ereditario (HEA), patologia rara, e di altre forme di angioedema
- Analizzare i tipi di trattamento effettuato e le tempistiche di permanenza in Osservazione Breve Intensiva.

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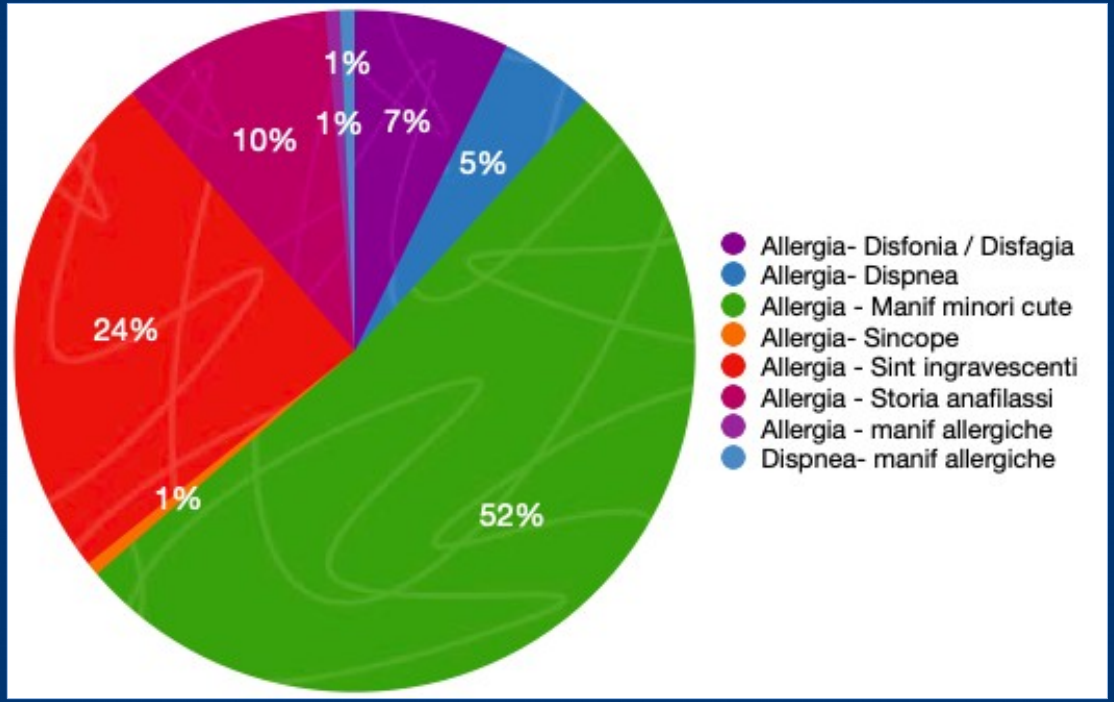
ANNI 2018 – 2019

Accessi totali in PS
150.701

Allergia al Triage 2.828
(1,8%)

CODICE	
Rosso	21 (0,7%)
Giallo	821 (29%)
Verde	750 (27%)
Bianco	430 (15%)



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DIAGNOSI CODIFICATE 2018 – 2019

1.535 casi totali 25 RICOVERI

DIAGNOSI	Totali	Ricoveri
Allergia	831	9
Angioedema	158	5
Edema laringe / faringe	35	4
Orticaria	447	3
Shock anafilattico	26	7

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ANGIOEDEMA IN PS UDINE 2018 – 2019

DIAGNOSI	Totali	Ricoveri
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Angioedema	158	5
Edema laringe / faringe	35	4
Orticaria	447	3
Shock anafilattico	26	2

Femmine 105 (54%)
Maschi 88 (46%)

Età media 56 anni

Ricoverati 4,7% (9) età media 83 anni

Dimessi età media 56 anni

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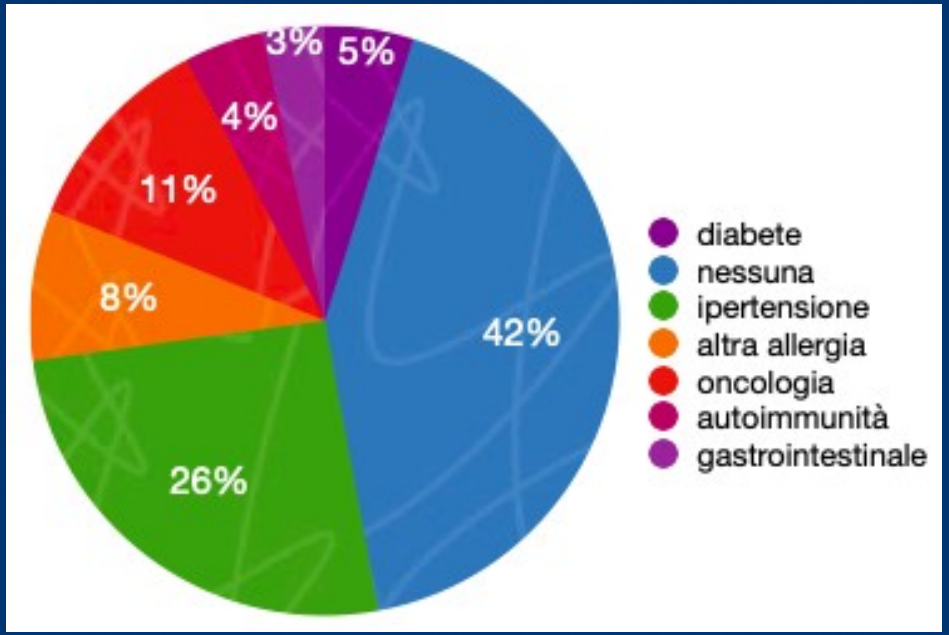
ANGIOEDEMA IN PS UDINE 2018 – 2019



Anamnesi di angioedema 35% (68)
di cui ereditario 1 caso (0,5%) !?

Primo riscontro 65% (125)

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ANGIOEDEMA e IPERTENSIONE

PATOLOGIE ASSOCIATE	Totali	% sui casi
Nessuna	87	42%
Ipertensione	53	26%
Altra allergia	17	8%
Oncologica	23	11%
Autoimmuni	9	4%
Gastrointestinale	7	3%

Utilizzano ACE-i (33)

17% dei casi di angioedema

67% degli ipertesi con angioedema

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ANGIOEDEMA e IPERTENSIONE

Table 1. Types of angioedema.

Types	Characteristics
Histamine-mediated (with urticaria)	- Allergy to food, venom, latex, medication - Acute or chronic spontaneous urticaria - Urticaria/angioedema associated with cold urticaria, vasculitis, exercise, episodic angioedema, vibration-induced, drug reaction
Bradykinin-mediated (without urticaria)	- Type I HAE: defective C1-INH level/function - Type II HAE: defective C1-INH function - Type III HAE: normal C1-INH -Acquired C1-INH deficiency: Type I associated with increased catabolism of C1-INH (lymphoproliferative disorder, autoimmune disease); Type II associated with autoantibody to C1-INH - ACEi-mediated angioedema - Medication associated: dipeptidyl peptidase-IV inhibitor (gliptins for diabetes mellitus), angiotensin II receptor blockers, recombinant tissue plasminogen activator, sirolimus, tacrolimus, everolimus
Idiopathic (unknown etiology)	- Histaminergic - Nonhistaminergic

HAE, hereditary angioedema; *C1-INH*, C1 inhibitor; *ACEi*, angiotensin-converting enzyme inhibitor.

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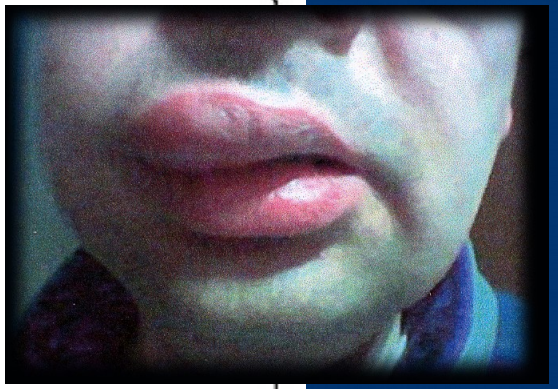
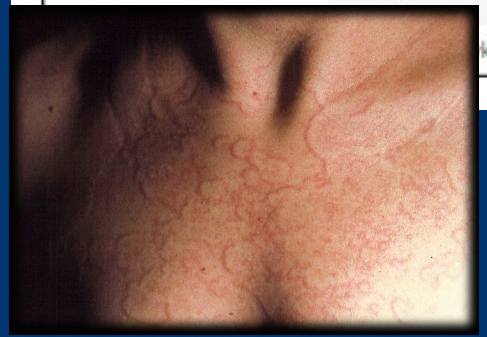
Histamine mediated	Bradykinin mediated
	Swelling of lips/tongue
Urticaria	
Itching	
	Laryngeal swelling
	Facial swelling
Rapid onset	Abdominal pain
Response to epinephrine	Abdominal swelling
	Nausea and vomiting
Hypotension/shock	Peripheral swelling
Wheeze	Genitourinary swelling

kinin-mediated angioedema





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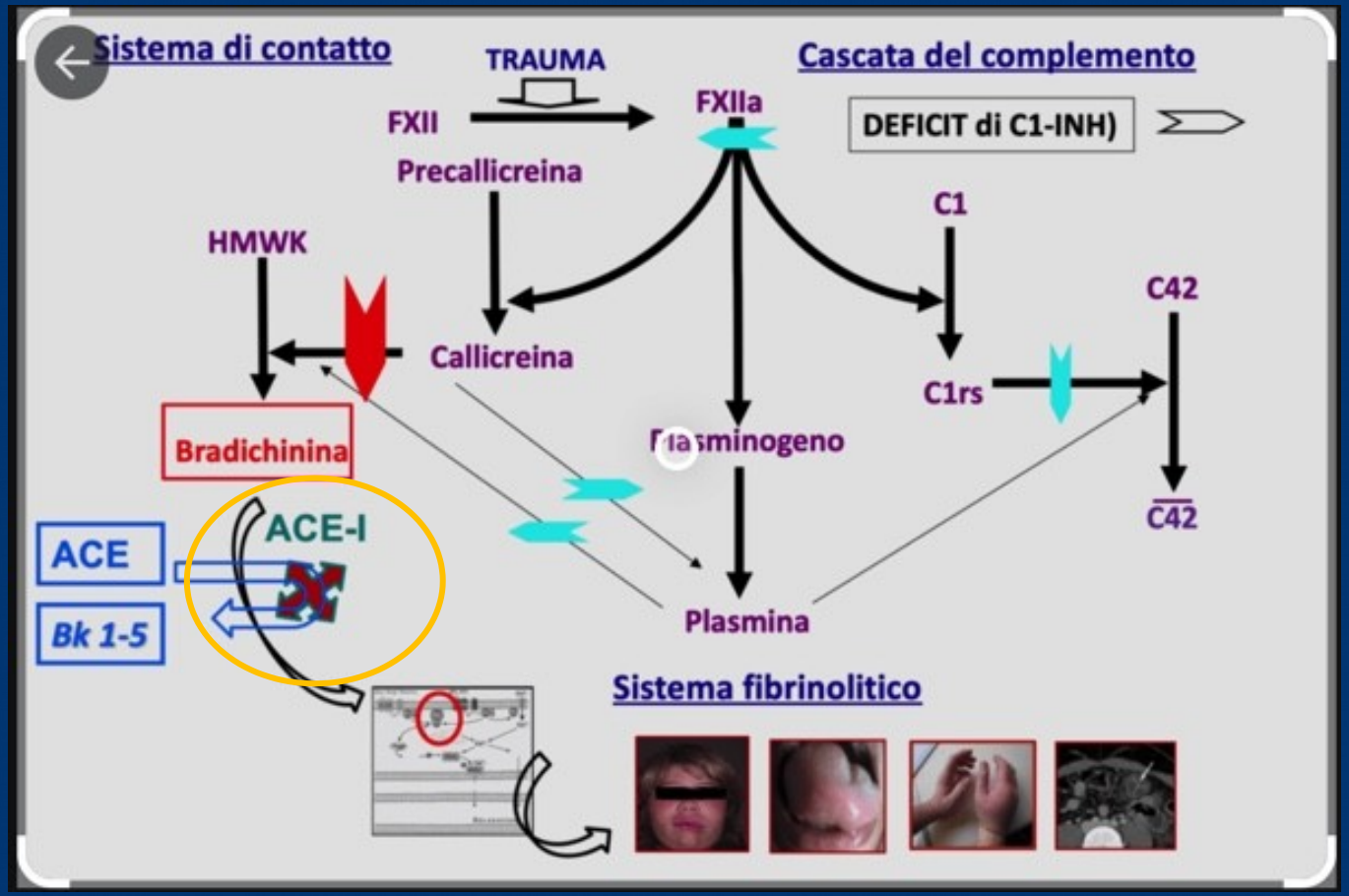

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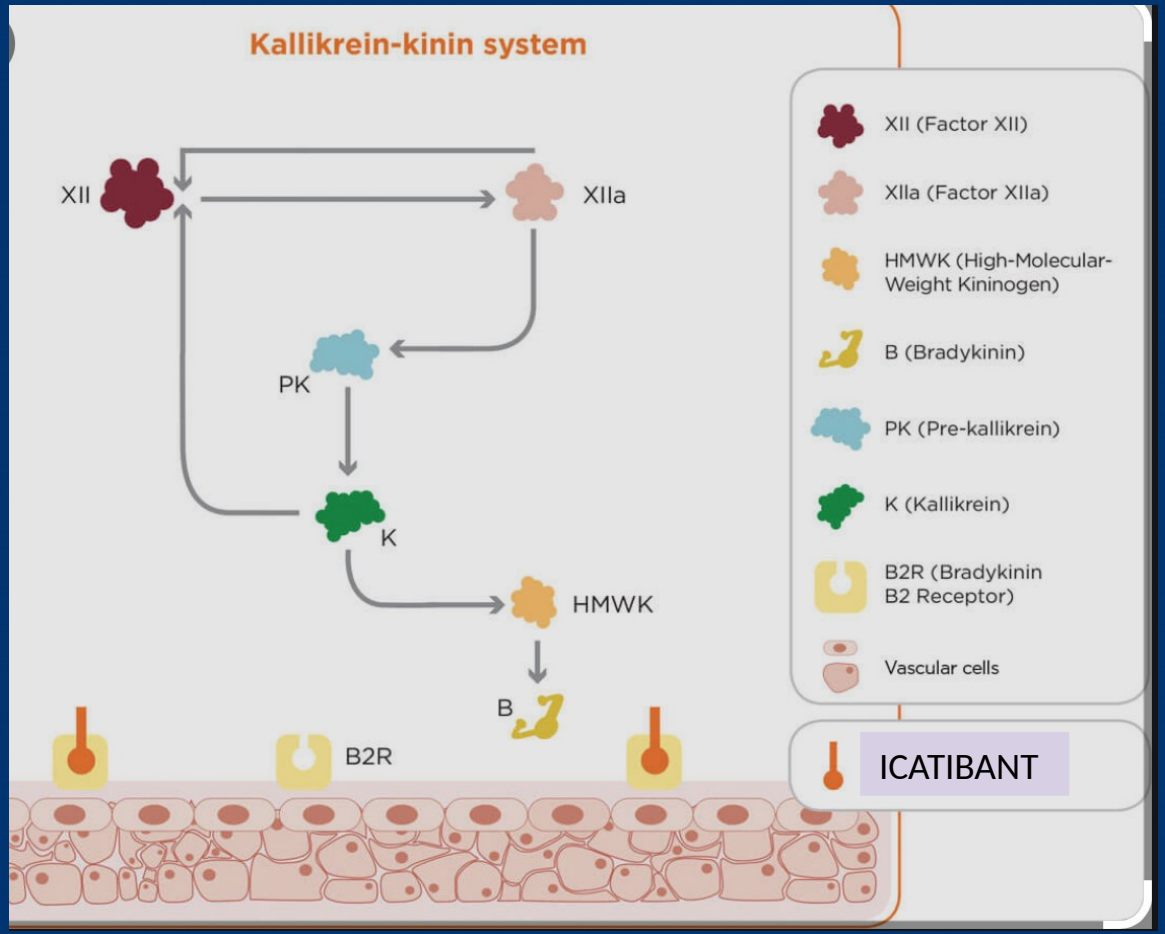
Kallikrein-kinin system
XII
XIIa
PK
K
HMWK
B
B2R
XII (Factor XII)
XIIa (Factor XIIa)
HMWK (High-Molecular-Weight Kininogen)
B (Bradykinin)
PK (Pre-kallikrein)
K (Kallikrein)
B2R (Bradykinin B2 Receptor)
Vascular cells
ICATIBANT

ANGIOEDEMA IN PS UDINE 2018 – 2019

OPZIONI TERAPEUTICHE	Totali	% sui casi
Adrenalina	33	17%
Steroide	141	73%
Antistaminico	79	41%
Icatibant	5	2%

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OFF LABEL

Original Article

Randomized Trial of Icatibant for Angiotensin-Converting Enzyme Inhibitor–Induced Upper Airway Angioedema

Richard Sinert, DO[a], Phillip Levy, MD, MPH[b], Jonathan A. Bernstein, MD[c], Richard Body, MB ChB, PhD[d], Marco L.A. Sivilotti, MD, MSc[e], Joseph Moellman, MD[f], Jennifer Schranz, MD[g], Jovanna Baptista, MS[h], Alan Kimura, MD, PhD[i], and Wolfram Nothaft, MD[j]; on behalf of the CAMEO study group* *Brooklyn, NY; Detroit, Mich; Cincinnati, Ohio; Manchester, United Kingdom; Kingston, ON, Canada; and Lexington, Mass*

RESULTS: A total of 121 subjects were randomized (icatibant, n = 61; placebo, n = 60); 118 received treatment a median of 7.8 hours from symptom onset. We observed no difference in time to meeting discharge criteria between groups (median, 4.0 hours in each group; $P = .63$). There also was no difference in time to onset of symptom relief (median, icatibant, 2.0 hours; placebo, 1.6 hours; $P = .57$) or any other secondary end point. Similar findings were noted in prespecified and post hoc subgroup analyses stratified by symptom severity, time interval to treatment, age, and other clinical covariates. No new safety signals were detected.

CONCLUSIONS: Icatibant was no more efficacious than placebo in at least moderately severe ACE-I–induced angioedema of the upper airway. © 2017 Shire HGT Inc.,

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Icatibant in ACE-Inhibitor–Induced Angioedema

Murat Baş, M.D., Jens Greve, M.D., Klaus Stelter, M.D., Miriam Havel, M.D., Ulrich Strassen, M.D., Nicole Rotter, M.D., Johannes Veit, M.D., Beate Schossow, Alexander Hapfelmeier, Ph.D., Victoria Kehl, Ph.D., Georg Kojda, Pharm.D., Ph.D., and Thomas K. Hoffmann, M.D.

ABSTRACT

BACKGROUND
Angioedema induced by treatment with angiotensin-converting–enzyme (ACE) inhibitors accounts for one third of angioedema cases in the emergency room; it is usually manifested in the upper airway and the head and neck region. There is no approved treatment for this potentially life-threatening condition.

METHODS
In this multicenter, double-blind, double-dummy, randomized phase 2 study, we assigned patients who had ACE-inhibitor–induced angioedema of the upper aerodigestive tract to treatment with 30 mg of subcutaneous icatibant, a selective bradykinin B2 receptor antagonist, or to the current off-label standard therapy consisting of intravenous prednisolone (500 mg) plus clemastine (2 mg). The primary efficacy end point was the median time to complete resolution of edema.

RESULTS
All 27 patients in the per-protocol population had complete resolution of edema. The median time to complete resolution was 8.0 hours (interquartile range, 3.0 to 16.0) with icatibant as compared with 27.1 hours (interquartile range, 20.3 to 48.0) with standard therapy (P=0.002). Three patients receiving standard therapy required rescue intervention with icatibant and prednisolone; 1 patient required tracheotomy. Significantly more patients in the icatibant group than in the standard-therapy group had complete resolution of edema within 4 hours after treatment (5 of 13 vs. 0 of 14, P=0.02). The median time to the onset of symptom relief (according to a composite investigator-assessed symptom score) was significantly shorter with icatibant than with standard therapy (2.0 hours vs. 11.7 hours, P=0.03). The results were similar when patient-assessed symptom scores were used.

CONCLUSIONS
Among patients with ACE-inhibitor–induced angioedema, the time to complete resolution of edema was significantly shorter with icatibant than with combination therapy with a glucocorticoid and an antihistamine. (Funded by Shire and the Federal Ministry of Education and Research of Germany; ClinicalTrials.gov number, NCT01154361.)

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J Allergy Clin Immunol. 2017 July ; 140(1): 242–248.e2. doi:10.1016/j.jaci.2016.09.051.

Effect of bradykinin receptor antagonism on ACE inhibitor-associated angioedema

Brittany T. Straka, M.D.[1], **Claudia E. Ramirez, M.D.**[1], **James B. Byrd, M.D., M.S.**[1], **Elizabeth Stone, R.N.**[1], **Alencia Woodard-Grice, Ph.D.**[1], **Hui Nian, M.S.**[2], **Chang Yu, Ph.D.**[2], **Aleena Banerji, M.D.**[3], and **Nancy J. Brown, M.D.**[1]

[1]Department of Medicine, Vanderbilt University Medical Center, Nashville, TN 37232, USA

[2]Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN 37232, USA

[3]Massachussetts General Hospital, Boston, MA 02114

Conclusions—This study does not support clinical efficacy of a bradykinin B_2 receptor antagonist in ACE inhibitor-associated angioedema.

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DOI: 10.1111/jcpt.12997

REVIEW ARTICLE

Journal of Clinical Pharmacy and Therapeutics WILEY

Effect of icatibant on angiotensin-converting enzyme inhibitor-induced angioedema: A meta-analysis of randomized controlled trials

Jinyoung Jeon MSc[1,2] | Yun Jeong Lee PharmD, PhD[3] | Seok-Yong Lee PhD[1]

Results and discussion: A total of 234 records were identified after searching the databases. In total, three RCTs involving 179 patients were included in the meta-analysis. The three RCTs had a low risk of bias and the characteristics of the participants and the outcome measures were similar among the RCTs. Treatment with icatibant shortened the time to achieve complete resolution of ACEI-induced AE symptoms compared to placebo or conventional treatments. However, the difference was not statistically significant (MD: −7.77 hours; 95% CI: −25.18-9.63 hours). There were no differences between groups in terms of drug-related adverse effects, apart from the reactions at the site of injection (RR: 1.35; 95% CI: 0.53-3.45).

What is new and conclusion: This meta-analysis evaluated the effectiveness and tolerability of icatibant therapy for ACEI-induced AE, but the benefit of icatibant therapy over placebo or conventional treatment strategies could not be shown.

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ANGIOEDEMA IN PS UDINE 2018 – 2019

Tempi PERMANENZA in PS/OBI	Ore
Tempo medio dei casi	4,10
Icatibant	5,2
Steroide	3,5
Adrenalina	7

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REVIEW Open Access

Angioedema in the emergency department: a practical guide to differential diagnosis and management

Jonathan A. Bernstein[1*], Paolo Cremonesi[2], Thomas K. Hoffmann[3] and John Hollingsworth[4]

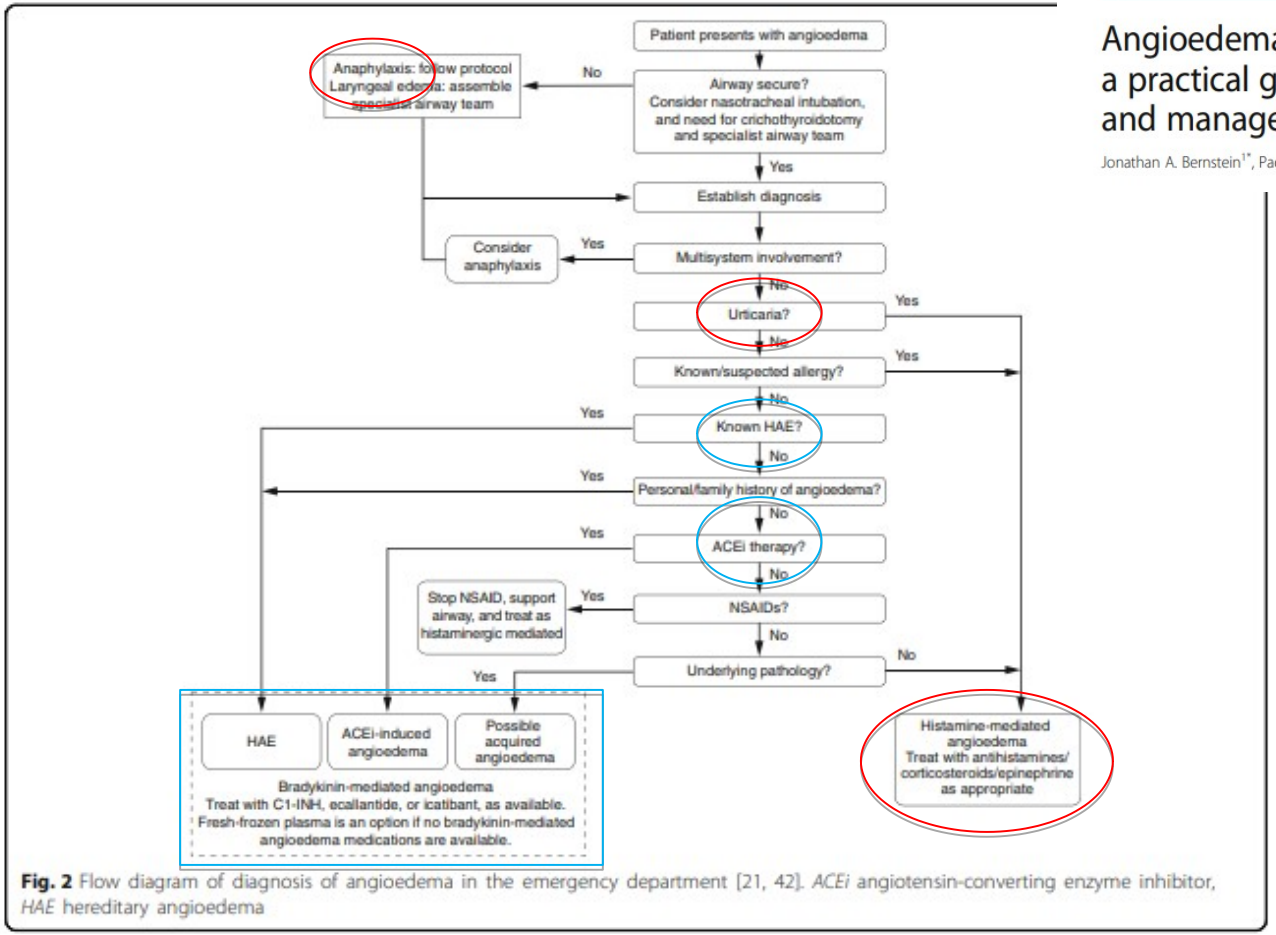

Fig. 2 Flow diagram of diagnosis of angioedema in the emergency department [21, 42]. *ACEi* angiotensin-converting enzyme inhibitor, *HAE* hereditary angioedema

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Table 2 Targeted treatment of HAE [21, 63–66]

Drug	FDA-approved indication	Mechanism of action	Dose/route/ price*	Time to onset of symptom relief	Adverse effects
Plasma-derived C1-INH (Berinert)	Acute abdominal, facial, or laryngeal HAE attacks in adult and pediatric patients (no lower age limit established)	C1-INH protein replacement	20 units/kg IV $8991 (1500 units)	Median: 48 min	Common: dysgeusia Rare: anaphylaxis, thrombosis Theoretical: blood-borne infections
Plasma-derived C1-INH (Cinryze)	Prophylaxis of HAE attacks in adults and pediatric patients ≥11 years of age	C1-INH protein replacement	1000 units IV $5704 (1000 units)	Median: 30 min	Common: dysgeusia Rare: anaphylaxis, thrombosis Theoretical: blood-borne infections
Recombinant C1-INH (Ruconest)	Acute HAE attacks in adults and pediatric patients ≥11 years of age; effectiveness not established for laryngeal attacks	C1-INH protein replacement	50 units/kg IV $12,142 (4200 IU)	Median: 90 min	Common: sinusitis, rash, pruritus Rare: anaphylaxis
Ecallantide (Kalbitor)	Acute HAE attacks in patients ≥12 years of age	Plasma-kallikrein inhibitor	30 mg SC $14,090 (30 mg)	Median: 67 min	Common: headache, nausea, pyrexia, injection site reactions Uncommon: anaphylaxis (must be administered by a health care professional)
Icatibant (Firazyr)	Acute HAE attacks in adults ≥18 years of age	Bradykinin-2 receptor antagonist	30 mg SC $10,037 (30 mg)	Median: 2 h	Common: injection site reactions, pyrexia, increased transaminases, dizziness Theoretical: worsening of an ongoing ischemic event

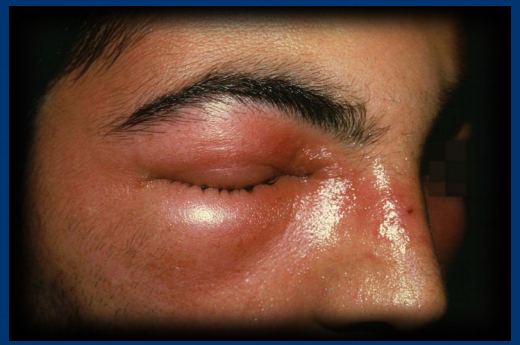
*US retail pricing obtained from www.drugs.com on April 5, 2017

CONCLUSIONI

- L'ANGIOEDEMA EREDITARIO E' UNA PATOLOGIA RARA CHE DEVE ESSERE CONOSCIUTA DAL MEDICO DI EMERGENZA

- IL SOSPETTO CLINICO DEVE SORGERE IN CASO DI ANGIOEDEMA **SENZA** ORTICARIA, NON RESPONSIVO ALLA TERAPIA CORTICOSTEROIDEA / ANTISTAMINICA / ADRENERGICA (PARTICOLARE ATTENZIONE SE ASSOCIATO DOLORE ADDOMINALE E/O CEFALEA)

- IN OGNI PS DEVE ESSERE PRESENTE LA POSSIBILITA' DI EFFETTUARE UNA TERAPIA SPECIFICA



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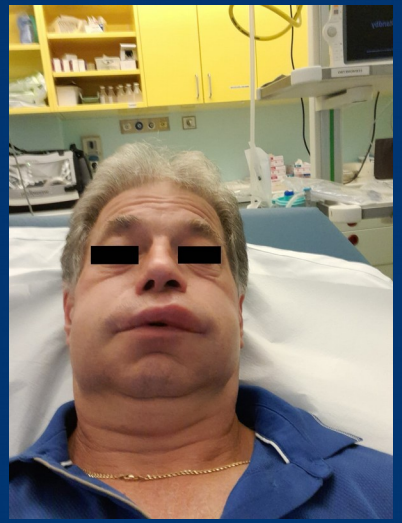
CONCLUSIONI

- L'ASSOCIAZIONE AD ASSUNZIONE DI ACE-i E' MOLTO FREQUENTE. QUINDI E' DOVEROSO RICORDARSI DI CONSIGLIARE UNA MODIFICA TERAPEURICA ALTERNATIVA ALL'ACE-i IN QUESTI PAZIENTI

- L'UTILIZZO DELL'ICATIBANT NELLE FORME DI ANGIOEDEMA DA ACE-i PUO' ESSERE CONSIDERATO, come nelle altre forme bradikinino-mediate



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GRAZIE

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