Angiotensin-converting-enzyme inhibitor–induced angioedema

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1 Angiotensin-converting-enzyme (ACE) inhibitors are the leading cause of drug-induced angioedema

Angiotensin-converting-enzyme (ACE) inhibitors are responsible for 20%–40% of emergency department visits for angioedema.[1] The incidence of ACE inhibitor–induced angioedema is about 0.1%–0.7% in the first 5 years of treatment; symptoms occur within the first month in 10% of cases.[1] Risk factors include concomitant use of dipeptidyl peptidase-4 inhibitors (e.g., sitagliptin), mammalian target of rapamycin (mTOR) inhibitors (e.g., sirolimus) and neprilysin inhibitors (e.g., sacubitril) (Appendix 1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.202308/tab-related-content).[1] Nonsteroidal anti-inflammatory drugs and statins can exacerbate angioedema, and the risk of ACE inhibitor–induced angioedema is fivefold higher in Black people.[2]

2 Common symptoms include facial, lip, tongue and upper airway swelling

Symptoms characteristically develop over the course of several hours. The absence of urticaria or pruritus distinguishes ACE inhibitor–induced angioedema from histamine-mediated angioedema.[2] Gastrointestinal manifestations such as abdominal pain or diarrhea are uncommon.[2]

3 Airway compromise is a life-threatening consequence of ACE inhibitor–induced angioedema

Patients should be monitored for at least several hours in the emergency department for symptom progression. About one-third of patients presenting with ACE inhibitor–induced angioedema require monitoring in the intensive care unit (ICU), and about 10% of patients require intubation.[2] Anesthesiology of otolaryngology should be involved early on to help manage difficult airways. The location of edema can aid disposition decisions; patients with tongue or laryngeal edema require ICU monitoring, and those with isolated lip, face or soft palate edema may be discharged or monitored on an inpatient unit.[3]

4 Stopping the ACE inhibitor is the most important treatment

Symptoms are typically self-limiting and resolve spontaneously 48–72 hours after stopping the ACE inhibitor.[2] Corticosteroids, antihistamines and epinephrine (used for histaminergic angioedema) are generally ineffective for ACE inhibitor–induced angioedema.[2] Randomized trials do not support the use of bradykinin receptor antagonists (icatibant) and kallikrein inhibitors (ecallantide).[1,4] Fresh frozen plasma and C1-inhibitor concentrate have reportedly reduced symptom duration in case studies, but have not been tested in trials.[1,4]

5 Angiotensin receptor blockers can be used if there is a clinical indication for renin–angiotensin–aldosterone system blockade

More than 40% of patients experience recurrence of angioedema despite stopping ACE inhibitors, usually within the first month.[1] Angiotensin receptor blockers act independently of the kinin–kallikrein system (Appendix 1) and do not increase the risk of angioedema in patients with previous ACE inhibitor–induced angioedema.[5]

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