

DOGMA DETECTIVES Case # 02-17-13-02: ANGIOEDEMA CHALLENGES

Are there any medications that can reverse medication (i.e. ACE inhibitor or calcium channel blocker) induced or hereditary angioedema? What treatment options are available for these non-allergic induced conditions?

Standard medications (epinephrine, steroids, antihistamines) WILL NOT have an effect in medication induced or hereditary angioedema.

Medication induced angioedema (from ACE inhibitors like lisinopril, and calcium channel blockers like amlodipine) is a process that is mediated by the inflammatory marker BRADYKININ and not by histamine. Hence, the common treatments used for allergic angioedema (which is histamine mediated) – including epinephrine, antihistamines (diphenhydramine and famotidine), and steroids (methylprednisilone or dexamethasone) are not effective.

In medication induced angioedema, there is a direct inhibitory effect on the enzyme that breaks down bradykinin, a naturally occurring inflammatory and signaling molecule in the body. This causes levels of bradykinin to rise, and eventually can lead to angioedema. It is somewhat of a random event, and can occur at ANY TIME while on these medications. People are sometimes on these medications for years before an adverse effect is seen. Treatment is supportive, requiring airway control and withdrawal of the offending medication. Often antihistamines and steroids are given, but do not expect them to be markedly effective. Nebulized epi can also be tried when concerned for impending airway compromise. Many of these patients are elderly or have cardiovascular disease – IM epinephrine is NOT recommended as there is no benefit and there is a risk of causing cardiovascular harm. Advanced airway techniques – including fiber-optic intubation – may be needed if severe angioedema is present.

Hereditary angioedema is due to deficiency or dysfunction of the C1 inhibitor protein causing bradykinin levels to rise. First-line therapies for acute attacks of hereditary angioedema include purified or recombinant human C1 inhibitor, Ecallantide (a kallikrein-bradykinin inhibitor), or Icatibant (a bradykinin B2 receptor antagonist). Fresh frozen plasma, which has intrinsic bradykinin inhibitors can also be employed in the treatment of these episodes. (<http://www.uptodate.com/contents/treatment-of-acute-attacks-in-hereditary-angioedema> and <http://emedicine.medscape.com/article/135604-overview>) There is some consideration to using these treatments for medication induced angioedema, however these medications typically work over 24-48 hours, and this is the time frame in which the medication effect will naturally wane as it is cleared from the body. Hence they are rarely employed in acquired (medication induced) angioedema.

Remember – allergic angioedema DOES respond to steroids, epi, and antihistamines. When in doubt you will not do harm by giving these (expect for the caution using epi in elderly or those with cardiovascular disease). Rapid transport to advanced airway control is essential for good patient outcomes in all cases.