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### Angioedema: ACE-Inhibitors Adverse Reaction

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# Angioedema: ACE-Inhibitors Adverse Reaction

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## Introduction

Angiotensin-converting enzyme inhibitor (ACEI) medications are one of the leading causes of angioedema in the United States, also known as ACEI-RA (Chan & Soliman, 2015, p. 207). ACE inhibitors are among the most commonly prescribed medications worldwide because they are indicated for the management of hypertension, congestive heart failure, myocardial infarction, diabetic nephropathy, and chronic kidney disease (Chan & Soliman, 2015, p. 207). According to Spencer (2016), there are an estimated 40 million people taking ACE inhibitors for either hypertension or congestive heart failure (CHF). Angioedema is estimated to occur in 0.1%-0.7% of patients on ACE inhibitor therapy. Of those who present to the emergency department with angioedema, 35% of cases are attributed to ACEI. Additionally, one study concluded that African-Americans are three times more likely to develop ACEI-RA within six months of starting ACE inhibitor therapy (Spencer, 2016). 0.7% may seem like a small number, but that is about twenty-eight thousand patients a year. There are several risk factors for developing ACE inhibitor angioedema. The primary risk factor is being African-American. The female population, with a history of angioedema and chronic disease are all contributing factors. What may seem odd is that it does not matter how long a patient is taking the medication before they develop a reaction. Some patients have taken the medication for more than 20 years before they had a reaction. Understanding Angio-converting enzyme inhibitors are important for all parties involved. As a healthcare provider who is going to be writing prescriptions, it is paramount to know the patients' health background and how ACEI works on a cellular level. Only after obtaining all the correct information will the healthcare provider choose whether this medication is right for the patient. Do the risks outweigh the benefits or vice versa?

## Signs & Symptoms

ACE inhibitors are associated with a variety of signs and symptoms. The following, but not limited to, are some of them. The most common symptom is a cough. The patients should notify the health care provider immediately because they may be experiencing a potential reaction to the medication. According to Wadelius et al., (2014), the following are possible risk factors and side effects (p. 479).

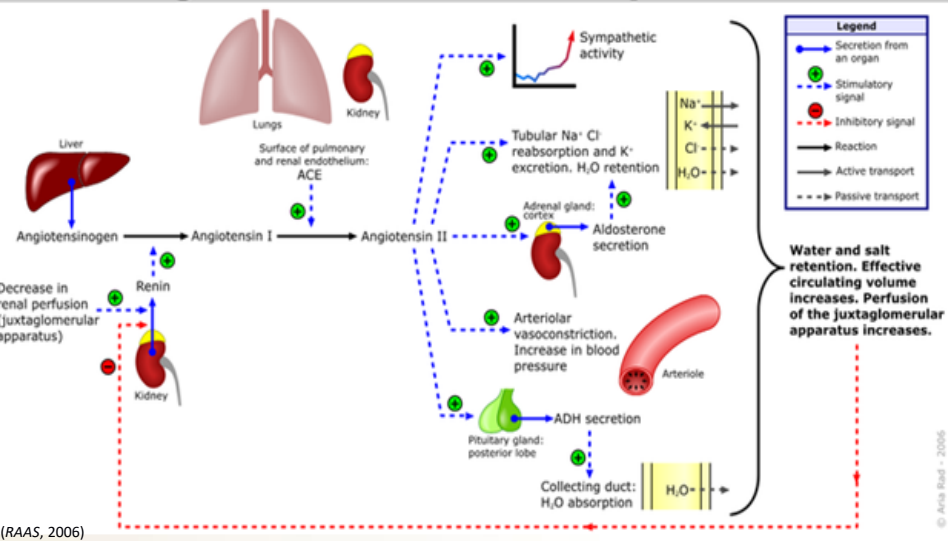
Signs & Symptoms
Cough
Swelling (maybe unilateral)
<ul style="list-style-type: none"><li>○ Face</li><li>○ Lips</li><li>○ Tongue</li><li>○ Floor of mouth</li><li>○ Larynx</li></ul>
Shortness of Breath
Difficulty Swallowing
Drizzling
Hoarse Voice
Risk Factors
Female Gender
African American
History of Angioedema
Advanced Age
Chronic Diseases (such as, heart failure, diabetes mellitus, coronary artery disease)
Hoarse Voice

(Wadelius et al., 2014, p. 479)



("Picture," n.d.)

## Renin-angiotensin-aldosterone system



## Underlying Pathophysiology

Angioedema is a potentially life-threatening adverse effect of ACE inhibitors, with a reported incidence of 0.1 to 6%. ACE-inhibitor-related angioedema is asymmetric, nonpitting, nontender edema that can appear anywhere on the body but commonly affects the head and neck area (Chan & Soliman, 2015 (p. 207). According to Chan and Soliman (2015), ACEI-RA is not considered a true allergic reaction but is considered an adverse class effect secondary to the mechanism of action (p. 207). A true allergic reaction would involve IgE antibodies. Interestingly, ACEI-RA is not IgE mediated; the physiology of the condition is caused by the levels of the blood vessel-dilating peptide bradykinin in the body (Spencer, 2016). Bradykinin counterbalances the vasoconstrictive workings of the renin-angiotensin-aldosterone system and is thought to be a primary mediator in nonallergic angioedemas (Spencer, 2016). ACE inhibitors, medications with a -pril suffix (e.g., captopril, lisinopril [Prinivil®],

fosinopril [Monopril®]), lower blood pressure by inhibiting the action of angiotensin-converting enzyme, thus interrupting the conversion of angiotensin I to angiotensin II (a potent vasodilator) and aldosterone (Wilson et al., 2014; Wynn & Maxey, 2012). ACE inhibitors also prevent the breakdown of the enzyme bradykinin (Fellicida-Reynaldo & Kenneally, 2015, p. 180). Bradykinin in low doses causes vasodilation, which potentiates the action of ACE inhibitors to lower blood pressure (Fellicida-Reynaldo & Kenneally, 2015, p. 180).

## Significance of Pathophysiology

Understanding how the pathophysiology of Angiotensin-converting enzyme inhibitor (ACEI) is essential in deciding if this medication is correct to resolve the patient's hypertension. This medication can lead to severe swelling, possible intubation or even tracheostomy placement. Patients with allergic emergencies presenting to an ED often receive medications including epinephrine,

antihistamines, and corticosteroids. Because ACEI angioedema is not mediated by mast cell degranulation, the efficacy of these medications remains controversial (Winter, Rosenbaum, Vilke, & Almazroua, 2013, p. 777). According to Scalese & Reinaker (2016), a medication called icatibant (Firazyr), which is administered only once subcutaneously at a dose of 30mg, has proven to be extremely successful in treating ACEI-RA. How this medication works is by blocking the bradykinin at the B2 receptor site. By doing this the vasodilation effects of bradykinin are rendered ineffective, thus decreasing the swelling. Icatibant works within minutes of administration and can prevent invasive procedures that otherwise, may be needed to ensure an effective airway (Scalese & Reinaker, 2016, p. 876) The downside to this medication is that it costs \$10,000 to \$12,000 per dose. This author believes that there is no amount of money you can put on someone's life. A night in the intensive care unit will cost much more. Fresh frozen plasma, C1 inhibitor, and icatibant appear to be safe and effective options for treating ACE

inhibitor-induced angioedema, whereas antihistamines and corticosteroids do not target the underlying mechanism (Scalese & Reinaker, 2016, p. 874).

## Implications for Nursing Care

ACE inhibitor angioedema is a relatively common side effect. These side effects could be seen in all clinical care settings. As the bedside nurse, it is important to be able to recognize the signs and symptoms of ACEI-RA quickly. As an Advanced Practicing Provider, it will be imperative to know these patients will not present like a typical allergic reaction i.e. itching, urticaria. These patients will not be treated in the same allergic reaction manner. Emergency room nurses need to recognize these patients as immediate life threats and should be seen immediately. Patients being seen outside of the Emergency room will need to be taken to the Emergency room by EMS. Advanced practice nurses will need to be aware of the risk factors involved in prescribing an ACEI to their patients. If the risk factors are too high, the provider will need to consider an alternate medication. The early warning sign of a reaction is a chronic cough. All patient will need to be educated extensively about the signs and symptoms of angioedema. Written literature will be very helpful for the patient to take home.

## Conclusion

ACEIs are very effective in treating chronic diseases. APPs must be vigilant in screening their patients as well as their family members (if possible) before prescribing these medications. Nurses and APPs will need to provide educational material patients. The health and wellness of each patient is essential. This author wants to educate the community on the signs and symptoms of ACEI-RA as well as the pathophysiology.

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