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Angioedema: Adverse Reaction from ACE-Inhibitors

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Introduction

Angiotensin-converting enzyme inhibitor (ACE) medications are one of the leading causes of angioedema in the United States, also known as ACEI-RA (Chan & Soliman, 2015). ACE medications are frequently prescribed to help manage diseases, such as hypertension and congestive heart failure, and include, but are not limited to lisinopril and enalapril, with lisinopril being the most commonly prescribed at this time (Chan & Soliman, 2015). In addition, ACEIs are used to help prevent myocardial infarction, diabetic neuropathy, and a cerebrovascular accident (Chua, Ignaszewski, & Schwenger, 2011).

According to Loftus et al. (2014), about 40 million people were taking ACEIs in 2000, with ACEI-RA resulting in only "0.1%-6% of cases" (p. 2506). Less than six percent sounds like a rather small number; however, with such a large population taking ACEIs, the potential cases of related angioedema amount upwards to two million patients (Loftus et al., 2014). There are several risk factors for developing ACEI-RA, with the greatest at risk group being African-American females, who are "three times more likely to develop ACEI-RA" (Spencer, 2016, p. 41). A list of known risk factors for developing ACEI-RA is provided in the next section. The length of time taking an ACEI does not determine if or when angioedema will occur. In a study by Chan and Soliman (2015), one patient took an ACEI for nearly 20 years without any signs of an adverse reaction, when that individual suddenly developed angioedema as a result of the ACEI.

The author of this research project has chosen angioedema caused by ACEI medications because it is seen frequently in the emergency department, which is the author's current area of practice. Understanding ACE-RA is important for all involved in direct patient care, particularly emergency medicine and those who have prescription privileges. When prescribing a drug from this class, one must understand the pharmacokinetics of ACEIs in the human body and the particular patient's risk factors for developing angioedema, then weigh the risks versus benefits in order to provide the best possible care to patients.

Signs & Symptoms

The following are possible signs and symptoms associated with ACEI-RA, with a cough being one of the first symptoms a patient may notice, and should be a warning sign to healthcare providers that the patient may be experiencing a potential reaction to the ACEI (Chan & Soliman, 2015, p. 92). Also, potential risk factors for developing ACEI-RA are provided below (Wadelius et al., 2014, p. 479).

Signs & Symptoms

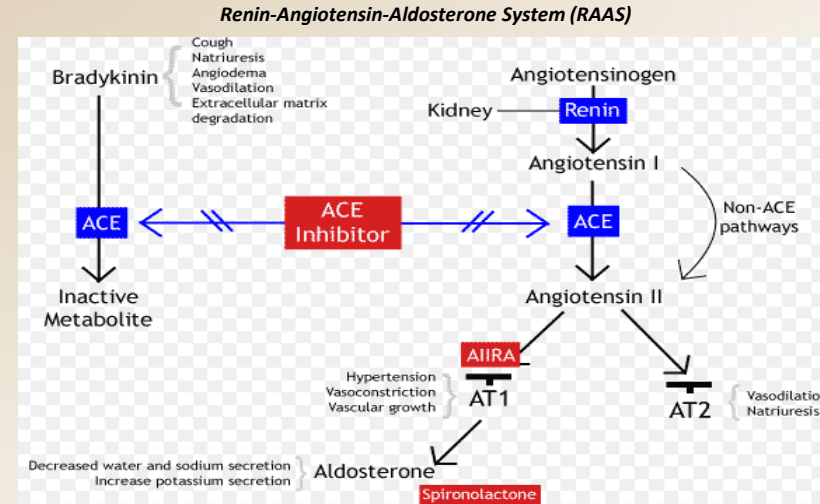
Cough
Swelling (may be unilateral)
<ul style="list-style-type: none">○ Face○ Lips○ Tongue○ Floor of mouth○ Larynx
Shortness of Breath
Difficulty Swallowing
Drizzling
Hoarse Voice

Risk Factors

Female Gender
African American
History of Angioedema
Advanced Age
Chronic Diseases (such as, heart failure, diabetes mellitus, coronary artery disease)
Hoarse Voice



(Thompson, 2010a)



(Bpac.org, 2016)

Underlying Pathophysiology

ACEI-RA is not considered a true allergic reaction, but is rather a potentially life threatening side effect from taking an ACEI (Chan & Soliman, 2015). A true allergic reaction is one that involves IgE antibodies, which ACEI-RA does not (Spencer, 2016). Angiotensin-converting enzyme (ACE) is an enzyme in the human body that helps to control and limit the manufacturing of bradykinin (Gang et al., 2013). It does so by blocking angiotensin I from converting to angiotensin II, which has vasoconstrictive activity in the body (Knecht, Dunn, & Macaulay, 2014). This process is part of a more complex system in the human body, known as the renin-angiotensin-aldosterone system (RAAS) (Fagyas et al., 2014). An algorithm is provided below, outlining the RAAS in further detail.

Bradykinin is involved in the innate immune system and works by causing vasodilation, and when left unchecked, ultimately results in angioedema (Maurer et al., 2011). When the activity of ACE is inhibited, bradykinin is able to accumulate, thus explaining why these medications can result in inadvertent angioedema (Gang et al., 2013). Untreated, ACEI-RA will resolve on its own within hours to days and is self-limiting, however, the potential for respiratory compromise leading to respiratory arrest is very high (Rasmussen, Mey, & Bygum, 2014).

Significance of Pathophysiology

Understanding the pathophysiology behind ACEI-RA is key to deciding a plan of care in order to resolve the patient's signs and symptoms, and prevent possible intubation or tracheostomy placement. While medications such as diphenhydramine, famotidine, epinephrine, and/or steroids are typical treatments for true allergic reactions, these medications are ineffective for ACEI-RA, because it is not mediated by IgE or histamines (Gang et al., 2013). A medication called icatibant, which is administered only once subcutaneously at a dose of 30 mg, has proven to be extremely successful in treating ACEI-RA (Scalese & Reinaker, 2016). It blocks the receptor for bradykinin at the B2 receptor site. In doing so, the vasodilator effects of bradykinin are rendered completely ineffective, thus reducing the swelling and other associated symptoms.

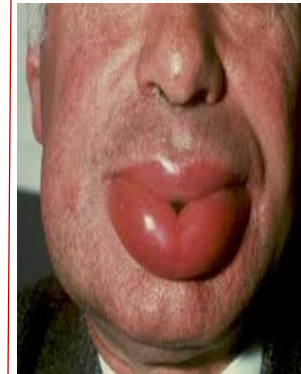
According to Scalese and Reinaker (2016), icatibant works within minutes of administration and can prevent invasive procedures that otherwise, may be needed to ensure an effective airway.

One noteworthy downside to icatibant is its' cost, which is approximately \$10,000 to \$12,000 (Scalese & Reinaker, 2016). However, the author's perspective is that the cost of this drug is significantly less than an intensive care unit admission, in addition to several other treatments and drugs that may be needed if angioedema is not quickly reversed. Other treatments that have proven to be less effective, but are worth considering if icatibant is unavailable are fresh frozen plasma and C1 inhibitors (Scalese & Reinaker, 2016).

Implications for Nursing Care

ACEI-RA is becoming a relatively common side effect, which has the potential to be seen in all clinical settings. Regarding bedside nursing, it is important to be able to promptly recognize the signs and symptoms of ACEI-RA, knowing that these patients will not present with itching, urticaria, et cetera, which are typically seen with allergic reactions (Cosco & Winawer, 2015). In the emergency department, nursing staff needs to be able to identify these patients as critical and immediately notify a healthcare provider about the patient.

Advanced practice nurses, particularly those who have prescriptive authority, need to be aware of the risk factors associated with developing ACEI-RA and regularly screen patients taking an ACEI for early warning signs, such as a chronic cough. If the risk for developing ACEI-RA is too high, the prescribed may want to consider an alternative drug. All patients taking ACEIs need to be thoroughly educated about the signs and symptoms of ACEI-RA and what to do if he/she notices any of them. Lastly, all clinical healthcare professionals need to be aware that ACEI-RA is not an allergic reaction and should not be treated as such. Medications, such as icatibant, should be used if available to improve patient outcomes.



(Thompson, 2010b)

Conclusion

ACEIs are highly effective for treating several chronic diseases that would otherwise have a much higher morbidity and mortality rate (Chua et al., 2011). Despite the positive benefits of this medication class, the deleterious effects of angioedema warrants vigilant screening of patients taking ACEIs by healthcare providers and promoting awareness in patients and close family members, if possible. The author strives to bring awareness to the signs, symptoms, and underlying pathophysiologic process of ACEI-RA.

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