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ACE inhibitors and ARBs: Understanding the basics

Through the exploration and understanding of a clinical scenario, you can safely administer ACE inhibitors and ARBs in daily clinical practice.

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Angiotensin-converting enzyme inhibitors, better known as ACE inhibitors, were first marketed in 1981 for the treatment of hypertension.[1] Since their introduction, ACE inhibitors have been widely used in patients with hypertension, heart failure, coronary artery disease, diabetes, nephrotic syndrome, and chronic kidney disease (CKD). With the generic name of most ACE inhibitors using the suffix "-pril," medications that are members of this class are similar in action and have like adverse reactions. Used alone or in combination with other medications to treat disease processes or to prevent complications of diseases, ACE inhibitors are one of the most prescribed classes of medication.[2]

Angiotensin II receptor blockers, also known as ARBs, were introduced in 1995 and are similar to ACE inhibitors in their mechanism of action and use.[1] Originally designed to be an alternative for patients experiencing ACE inhibitor-induced cough, ARBs are now used alone or in combination with other medications to treat hypertension, heart failure, and CKD.[3] Like their ACE inhibitor cousin, ARBs end with a special suffix, "-sartan," sharing actions and adverse reactions among the medications in this class (see *Common ACE inhibitors and ARBs*).[2]

Nurses and nursing students are likely to administer ACE inhibitors and ARBs daily in a variety of settings. Basic knowledge of the current uses, mechanisms of action, adverse reactions, nursing implications, and future medication considerations is necessary. Understanding the similarities and differences between ACE inhibitors and ARBs will allow you to safely administer and educate your patients on these medications. Throughout this article, we'll describe ACE inhibitors and ARBs through the application of the following case scenario to solidify your knowledge on these common medications.

Case scenario

A 56-year-old White female presents to the clinic to seek treatment for a nagging cough that's worsened over 2 weeks. The patient has a history of treatment for asthma and eczema since childhood. One month ago, she was diagnosed with type 2 diabetes and hypertension. Her primary care physician prescribed lisinopril 10 mg by mouth daily for treatment of hypertension and metformin 500 mg

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Common ACE inhibitors and ARBs

ACE inhibitors	ARBs
benazepril	eprosartan
captopril	irbesartan
enalapril	losartan
lisinopril	telmisartan
ramipril	valsartan

twice daily for treatment of diabetes, and she has been taking both medications as prescribed. Since taking the medications, her BP and blood glucose have been controlled, but she has developed a cough that won't go away. She also reports numbness and tingling in the feet bilaterally, mostly at night. Upon evaluation, breath sounds are clear to auscultation bilaterally with a respiratory rate of 18. No accessory muscle use or intercostal retractions are noted. A dry cough is present. Nonpitting edema is noted in the bilateral lower extremities.

The renin-angiotensin-aldosterone system

Let's start by understanding the normal function of the renin-angiotensin-aldosterone system, also known as RAAS. Renin is typically secreted by the kidneys when a drop in BP, reduction in sodium, or detection of sympathetic nervous system activity is noted. Physiologically, renin has little impact on the body other than to provide instructions to secrete angiotensin I. Like renin, angiotensin I has little physiologic effect on the body other than to provide instructions to secrete angiotensin II. Angiotensin II is a potent vasoconstrictor that aims to increase BP. Angiotensin II then provides instructions to secrete aldosterone, which enables the body to retain sodium. What follows sodium? Water. By increasing the amount of vascular constriction as well as retaining sodium and water, the overall BP is increased via two mechanisms. The more constriction and vascular volume present, the higher the BP.

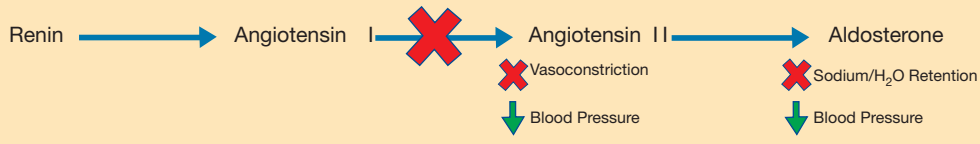
Mechanism of action: ACE inhibitors

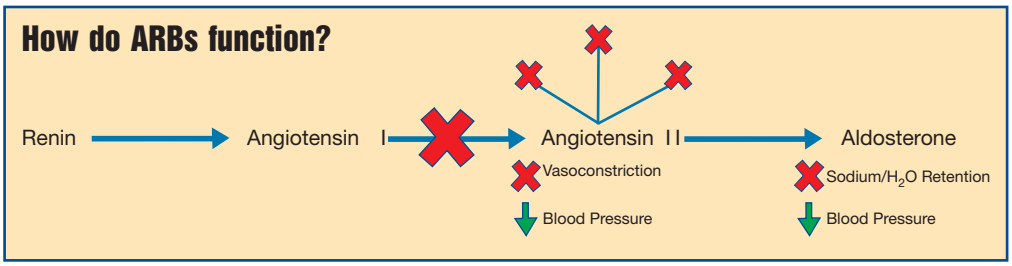
ACE inhibitors work primarily by altering the normal function of RAAS.[2] ACE inhibitors prevent the conversion of angiotensin I to angiotensin II, thus directly preventing the potent vasoconstriction and indirectly preventing sodium and water retention that are normally seen with RAAS activation (see *How do ACE inhibitors function?*). Without angiotensin II, there is no subsequent aldosterone. ACE inhibitors also stop the breakdown of bradykinin and substance P; both are potent vasodilators.[2] With ACE inhibitors, the BP is lowered by promoting vasodilation and increasing the excretion of sodium, followed by water. With greater vasodilation and lower vascular volume, the lower the BP. Now we can understand why the patient in the case scenario was prescribed lisinopril to treat her hypertension. With inhibition of the RAAS, the patient in the case study has achieved controlled BP.

Mechanism of action: ARBs

ARBs also work on the RAAS to help reduce BP but do so in a slightly different manner than an ACE inhibitor. Instead of

How do ACE inhibitors function?





preventing the conversion of angiotensin I to angiotensin II, ARBs block the binding of angiotensin II to specific angiotensin II receptors (see *How do ARBs function?*). This blockade prevents the vasoconstrictive effects of angiotensin II and indirectly blocks aldosterone, preventing sodium and water retention.[2] Of note, ARBs don't provide significant effects on bradykinin and substance P, another slight difference when compared with the ACE inhibitor class. The result is still the same: a reduction in BP through vasodilation and lower vascular volume.

Adverse reactions: ACE inhibitors

One of the most recognizable adverse reactions of ACE inhibitors is a nagging cough. Typically, the cough isn't accompanied by sputum production and can be seen as early as 1 week after the first dose. However, a nagging cough may first develop months after the initial dose. The cough usually subsides within a month of discontinuing ACE inhibitor therapy. Additionally, ACE inhibitor therapy may increase the risk of bronchospasm; ACE inhibitors should be used cautiously in patients with a concurrent diagnosis of asthma.[4]

Is the patient's cough in the case scenario related to her ACE inhibitor use? As noted, ACE inhibitors block the breakdown of bradykinin to help with vasodilation effects. In the lungs, this allows more bradykinin to be present, which causes bronchial irritation. This excessive bradykinin is suspected to cause the nagging cough associated with ACE inhibitors.[4]

Due to the therapeutic vasodilation effects of ACE inhibitors, hypotension, dizziness, and near-syncope are also commonly experienced. Although vasodilation and a reduced BP are expected as part of therapy, it may take the body time to adjust to this reduction in perfusion. This lowered BP reduces perfusion to the brain, resulting in hypotension, dizziness, and near-syncope. Fatigue is also commonly noted during the first few weeks of therapy as these vasodilation effects reduce perfusion to the body.[4]

ACE inhibitors may also cause elevations in serum potassium, blood urea nitrogen (BUN), and creatinine.[4] We know that ACE inhibitors alter the normal function of the RAAS, which is initiated in the kidneys. As the medication changes the function of the RAAS in the kidneys, the medication has the potential to cause renal insufficiency. BUN and creatinine are commonly measured to determine renal function, as high elevations indicate renal insufficiency. Identifying a reduction in glomerular filtration rate is also used to assist in determining renal insufficiency with ACE inhibitor use.[4]

Remember, aldosterone is indirectly blocked with ACE inhibitors as the conversion to angiotensin II is directly prevented. Aldosterone normally retains sodium. With ACE inhibitors, aldosterone is now blocked, causing sodium excretion in the urine. This lowered serum sodium causes serum potassium to increase as these two electrolytes are inversely related. As sodium goes down, potassium goes up, causing hyperkalemia.

Other common adverse reactions of ACE inhibitors include headache, rash, sexual dysfunction, and alterations in

Comparison of ACE inhibitor and ARB adverse reactions

Adverse reaction	ACE inhibitors	ARBs
Nagging cough	✓	✗
Hypotension	✓	✓
Headache	✓	✓
Dizziness	✓	✓
Near-syncope	✓	✓
Hyperkalemia	✓	✓
Renal insufficiency	✓	✓
Angioedema	✓	✗
Fetal toxicity	✓	✓

taste. All ACE inhibitors carry the risk of toxicity to the fetus. These medications should be avoided during pregnancy and for lactating women.[2]

ACE inhibitor-induced angioedema occurs in 0.1%-0.7% of patients, predominantly in the Black and Hispanic populations. Though rare, ACE-induced angioedema can be a serious adverse reaction.[5] Angioedema is categorized by swelling of the dermis, including the lips, tongue, airway, and other tissue. Life-threatening angioedema is thought to be caused by excessive bradykinin that promotes vasodilation and interstitial fluid shifts, creating edema. This edema compromises the patient's ability to maintain a patent airway. Discontinuation of the ACE inhibitor is the primary method of reversal.[4]

Adverse reactions: ARBs

As the mechanism of action for ARBs directly prevents angiotensin II and indirectly prevents aldosterone, the adverse reactions of hypotension, dizziness, near-syncope, headache, hyperkalemia, and renal insufficiency are similar to ACE inhibitors. ARBs don't have a significant effect on bradykinin; therefore, a nagging cough and angioedema with ARBs are rare. In fact, patients who experience a cough or angioedema with an ACE inhibitor are often switched to an ARB for the same therapeutic effect.[3] Now ask yourself: Should the patient in the case scenario discontinue her ACE inhibitor and be switched to an ARB?

Other adverse reactions of ARBs include chest pain, fatigue, hypoglycemia, diarrhea, urinary tract infections, anemia, and weakness. Like ACE inhibitors, ARBs and other drugs that affect the RAAS carry the risk of fetal toxicity. These medications should not be used during pregnancy or when lactating.[2] (See *Comparison of ACE inhibitor and ARB adverse reactions*.) Let's continue.

Nursing implications

Monitor for a dry, nonproductive cough, especially during the first month of ACE inhibitor therapy. Perform a thorough respiratory assessment to ensure that the cough isn't related to another disease, such as asthma, bronchitis, or an infective process. You may encourage the consumption of hard candy or cough lozenges if the patient describes an irritation in the throat. Advocate for the healthcare provider to discontinue the ACE inhibitor if the cough continues and encourage replacement with an ARB. Looking back to the case scenario, the ACE inhibitor should be discontinued and replaced with an ARB.

Dizziness, headache, fatigue, and measurable hypotension are common adverse reactions due to the vasodilatory effects of ACE inhibitors and ARBs. Patients are at risk for falls secondary to reduced perfusion to the brain.[6] Perform a standardized fall risk assessment and implement fall precautions per your facility's protocol. Monitor BP readings and notify the healthcare provider if the systolic BP falls below 100 mm Hg (this number may not apply to every patient depending on diagnosis; refer to the provider's prescription), or if the patient is symptomatic. Encourage patients and family members to measure and record BP readings at

home. Orthostatic BP measurements may be indicated, especially during initiation of treatment. As ACE inhibitors and ARBs don't directly work on cardiac function, routine measurement of the heart rate prior to administration isn't typically performed.

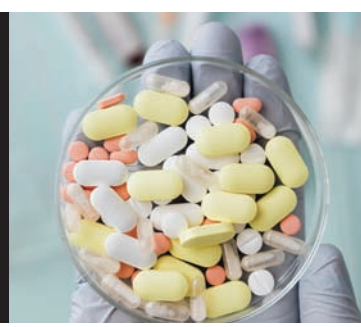
Review the patient's chemistry panel daily to monitor for hyperkalemia. Notify the healthcare provider if the patient's potassium level is greater than 5.0 mEq/liter before administering the medication, or per institutional guidelines. Assess the patient for symptoms of hyperkalemia that include muscle weakness, cramping, ECG changes, shortness of breath, palpitations, and arrythmias. Educate patients to avoid potassium-rich foods, such as oranges, bananas, melons, tomatoes, brussels sprouts, and dried fruits. Review the patient's medication record and notify the healthcare provider if potassium-sparing diuretics or nonsteroidal anti-inflammatory drugs are coprescribed with ACE inhibitors or ARBs.

Monitor the BUN, creatinine, and glomerular filtration rate as indicated to determine renal insufficiency. Maintain strict intake and output and notify the healthcare provider if urine output decreases or if the urine color and characteristics change. To assess for fluid volume overload, obtain a daily weight and assess for peripheral edema. The patient in the case scenario was noted to have nonpitting edema in the bilateral lower extremities. A detailed renal assessment should be performed to determine if she is developing renal insufficiency.

Educate women of child-bearing age regarding the risk of fetal toxicity with ACE inhibitor and ARB use. Encourage women to consult with their healthcare provider regarding birth control methods and risk/benefits of ACE inhibitor and ARB use. Typically, the medication is discontinued if the patient is pregnant or breastfeeding.

To monitor for the life-threatening complication of angioedema, assess for facial, tongue, lip, and peripheral swelling. Perform a detailed respiratory assessment to note wheezing, stridor, accessory muscle use, tachypnea, and decreased oxygen saturation and notify the healthcare provider if any of these symptoms are noted. If angioedema is detected, encourage the healthcare provider to discontinue the ACE inhibitor and initiate appropriate reversal therapy.

Educate women of child-bearing age regarding the risk of fetal toxicity with ACE inhibitor and ARB use. Encourage women to consult with their healthcare provider regarding birth control methods and risk/benefits.



ACE inhibitors and ARBs can be used for a variety of health conditions other than hypertension. Patients with heart failure and coronary artery disease can benefit from use as the vasodilatory effects reduce afterload and increase cardiac output, reducing workload of the heart. Patients with diabetes are at risk for developing diabetic nephropathy due to vascular injury from hyperglycemia. ACE inhibitors and ARBs are used to slow the development of diabetic nephropathy by reducing the amount of vascular injury via vasodilation. Similarly, patients may take ACE inhibitors and ARBs to slow the progression of CKD through vasodilation,

Consider this

A 65-year-old Black male presents to the ED with complaints of shortness of breath, fatigue, and intermittent palpitations. He states that his symptoms began last night after eating dinner. He has a past medical history of hypertension, diabetes mellitus type 2, and chronic back pain. The patient's home medication profile includes losartan 50 mg by mouth daily and ibuprofen 800 mg by mouth every 8 hours as needed. Upon assessment, oral temperature is 37 °C and his respiratory rate is 24, shallow in depth, with no accessory muscle use. Breath sounds are clear to auscultation bilaterally, and his SpO_2 is 96%. Cardiac S_1 and S_2 sounds are noted, and his heart rate is irregular at 58 beats/minute. Bilateral dorsalis pedis pulses are graded at 1+ in strength, with muscle strength 4/5 in all extremities.

A comprehensive metabolic panel, complete blood cell count, 12-lead ECG, and chest X-ray were prescribed and completed. Of note, the patient's potassium resulted at 5.7 mEq/liter and his ECG tracing showed sinus bradycardia with a rate of 57 beats/minute, including peaked T waves. The chest X-ray and other lab values were unremarkable.

In the case of this patient, the losartan, an ARB, is most likely causing hyperkalemia and the associated symptoms of fatigue, shortness of breath, and palpitations. The nurse should educate him on the typical signs and symptoms of hyperkalemia associated with ARB use and report those symptoms to the healthcare provider as soon as possible. Also, educate the patient to avoid high-potassium foods to assist in preventing hyperkalemia. Use of an ACE inhibitor or ARB, especially in combination with a nonsteroidal anti-inflammatory drug such as ibuprofen, increases the risk of developing hyperkalemia.[10] Communicate with the healthcare provider to consider prescribing the patient a nonopioid analgesic for his back pain, like acetaminophen, to avoid the risk of hyperkalemia.

maintaining renal perfusion. Through the maintenance of renal perfusion and glomerular filtration, ACE inhibitors and ARBs prevent proteinuria, and may be useful in patients experiencing nephrotic syndrome. During routine medication administration, educate your patients regarding the uses for ACE inhibitors and ARBs that may differ from the traditional treatment of hypertension.[2]

On the horizon

With the recent COVID-19 pandemic, questions regarding the continued use of ACE inhibitors and ARBs and the severity of COVID-19 infection have been noted.[7] It was hypothesized that patients taking ACE inhibitors and ARBs have an increased probability of contracting COVID-19 due to the readily available ACE binding receptors in the lungs. In addition, the known bradykinin effects of ACE inhibitor use may contribute to worsening cough and bronchospasm that can intensify the severity of COVID-19 infection.[8]

In a recent systematic review, however, there's supportive evidence that ACE inhibitors and ARBs don't worsen the severity of COVID-19 infection. In addition, there's no association between the use of these medications and a positive COVID-19 diagnosis. It's recommended that ACE inhibitors and ARBs are continued as prescribed with a concurrent COVID-19 diagnosis to maintain therapeutic effects. Patients diagnosed with COVID-19 who are taking an ACE inhibitor or ARB should be monitored closely for respiratory compromise. Studies with large sample sizes are recommended.[9]

Final overview

ACE inhibitors and ARBs are commonly prescribed for a variety of indications and are often seen in nursing practice. Through work on the RAAS, these medications help lower BP through vasodilation and excretion of sodium and water. You should be aware of major adverse reactions, including renal insufficiency,

hyperkalemia, and hypotension for both classes, and assess for these complications. ACE inhibitors carry the risk of producing a nagging cough and angioedema. As in the case scenario, patients with a nagging cough caused by an ACE inhibitor should be changed to an ARB. By understanding the basics of ACE inhibitors and ARBs, you can advocate for your patients if they experience unwanted or adverse events from these medications. ■

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