Angiotensin-Converting Enzyme inhibitors

Renin-Angiotensin-Aldosterone System

The RAAS is a critical hormonal cascade that regulates blood pressure, fluid balance, and systemic vascular resistance. Dysregulation of this system contributes significantly to the pathogenesis of hypertension, heart failure, and chronic kidney disease.

Key Components

1. **Renin**: An enzyme secreted by juxtaglomerular cells of the kidneys in response to:
    - Decreased arterial blood pressure
    - Reduced sodium chloride delivery to the distal tubule (sensed by the macula densa)
    - Increased sympathetic nervous system activity
2. **Angiotensinogen**: A glycoprotein produced by the liver, which is cleaved by renin to form angiotensin I.
3. **Angiotensin-Converting Enzyme (ACE)**: Primarily located on the endothelial cells of the lungs and kidneys, ACE converts angiotensin I to angiotensin II.
4. **Angiotensin II**: A potent vasoconstrictor that:
    - Increases systemic vascular resistance
    - Stimulates aldosterone secretion from the adrenal cortex
    - Promotes sodium and water reabsorption
    - Stimulates antidiuretic hormone (ADH) release
    - Enhances sympathetic nervous system activity
    - Induces thirst via central nervous system mechanisms
5. **Aldosterone**: A mineralocorticoid hormone that increases sodium and water reabsorption and potassium excretion in the distal nephron, contributing to increased blood volume and pressure.

Clinical Significance

Chronic overactivation of the RAAS can lead to:

- Left ventricular hypertrophy and remodeling
- Vascular endothelial dysfunction
- Progression of atherosclerosis
- Renal glomerular damage
- Increased cardiovascular morbidity and mortality

Angiotensin-Converting Enzyme (ACE) Inhibitors

Mechanism of Action

ACE inhibitors block the conversion of angiotensin I to angiotensin II, leading to:

- Reduced vasoconstriction
- Decreased aldosterone secretion
- Lowered sodium and water retention
- Increased bradykinin levels, promoting vasodilation
- Prevention of adverse cardiac remodeling

Therapeutic Indications

- Hypertension
- Heart failure with reduced ejection fraction (HFrEF)
- Post-myocardial infarction management
- Diabetic nephropathy
- Chronic kidney disease with proteinuria

Common ACE Inhibitors

- **Captopril**: Short-acting; requires multiple daily doses; food may reduce absorption.
- **Enalapril**: Prodrug converted to enalaprilat; longer half-life allows for once or twice-daily dosing.
- **Lisinopril**: Not a prodrug; long-acting; suitable for once-daily dosing; absorption not affected by food.
- **Ramipril**: Prodrug with tissue-specific activity; beneficial in heart and kidney protection.

Adverse Effects

- Dry, persistent cough (due to increased bradykinin)
- Hyperkalemia
- Hypotension, especially after the first dose
- Renal function deterioration in patients with bilateral renal artery stenosis
- Angioedema
- Taste disturbances
- Skin rashes

Contraindications

- Pregnancy (teratogenic effects)
- History of angioedema related to previous ACE inhibitor therapy
- Bilateral renal artery stenosis
- Hyperkalemia

Monitoring Parameters

- Blood pressure
- Serum potassium levels
- Renal function tests (serum creatinine and BUN)
- Signs of angioedema