Commentary

iMedPub Journals
www.imedpub.com

Molecular Enzymology and Drug Targets
ISSN 2572-5475

2021
Vol.7 No.2:1

Theoretical Basis Potential Interaction between Aspirin and Enalapril in Cardiovascular Patients

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Received date: October 1, 2021; **Accepted date:** October 15, 2021**; Published date:** October 22, 2021

Citation: Perry M (2021) Theoretical Basis of Potential Interaction between Aspirin and Enalapril in Cardiovascular Patients. Mol Enzy Drug Targ Vol: 7 No.2:1

Description

Aspirin

Aspirin is a commonly used drug to treat pain and fever. Acetylsalicylic acid has both anti-inflammatory and antipyretic effects. The drug also suppresses platelet aggregation and is used to prevent stroke and Myocardial Infarction (MI).

Aspirin mechanism

Acetyl-Salicylic Acid (ASA) blocks prostaglandin synthesis. Inhibition of COX1 leads to inhibition of platelet aggregation for approximately 7-10 days. Aspirin acetyl binds to the serine residue of the enzyme Cyclooxygenase 1 (COX1), causing irreversible inhibition. This prevents the production of pain-causing prostaglandins. This process also stops the conversion of arachidonic acid to thromboxane A2 (TXA2). It is a powerful inducer of platelet aggregation. Platelet aggregation can cause thrombosis and harmful venous and arterial thromboembolism, which can lead to conditions such as embolism and stroke.

Indications of aspirin for cardiovascular disease

- Aspirin therapy is very helpful for people with a history of CHD or stroke. Most heart attacks and strokes occur when the blood supply to the heart muscle or parts of the brain is cut off.
- Aspirin thins blood and prevents the formation of blood clots. It helps more blood flow to your feet. If you have an arrhythmia, you can treat the attack and stop the blood clot.

Enalapril

Enalapril is an ACE inhibitor that acts on the renin-angiotensin-aldosterone system, which is involved in the regulation of blood pressure and fluid and electrolyte homeostasis.

Enalapril mechanism

Angiotensin I is converted to angiotensin II by angiotensin converting enzyme (ACE). Angiotensin II constricts blood vessels and enhances important functions. Enalaprilat, the active metabolite of Enalapril, is an ACE inhibitor. Inhibition of ACE lowers angiotensin II levels, reduces vasoconstriction, and lowers blood pressure.

Indications for Enalapril in cardiovascular patients

- Enalapril is primarily used to treat hypertension.
- It is also used to treat Congestive Heart Failure (CHF).

Interaction between Aspirin and Enalapril

Aspirin (acetylsalicylic acid) and ACE inhibitors are often used at the same time. ACE inhibitors block the breakdown of bradykinin and vasodilator prostaglandins especially in patients with both heart failure and ischemic heart disease that causes heart failure. It stimulates the production and release of I2 and E2 from the endothelium to the peripheral circulation [1]. Salicylic acid inhibits the production of platelet cyclooxygenase and vasodilatory prostaglandins, especially in patients with hyponatremia in which the renin-angiotensin-prostaglandin system is overstimulated [2]. This property of salicylic acid can reduce the beneficial effects of ACE inhibitors in patients with congestive heart failure. Another product of the cyclooxygenase pathway is the potent prostaglandin thromboxane A2 (TxA2), which promotes blood clots and exhibits a vasoconstrictor effect. Some of the vasoconstrictor effects of angiotensin II are mediated by TxA2. Therefore, ACE inhibitors can partially develop vasodilatory effects by diminishing the production of this prostaglandin. Similarly, salicylic acid inhibits the production of cyclooxygenase enzyme and TxA2. Because ACE inhibitors and salicylates appear to have comparable endpoints (i.e., reduced TxA2 production), the addition of cyclooxygenase inhibitors such as aspirin to ACE inhibitor therapy may not induce any further benefit over ACE inhibitors alone. On the other hand, using both drugs at the same time can potentiate each other (Figure 1).

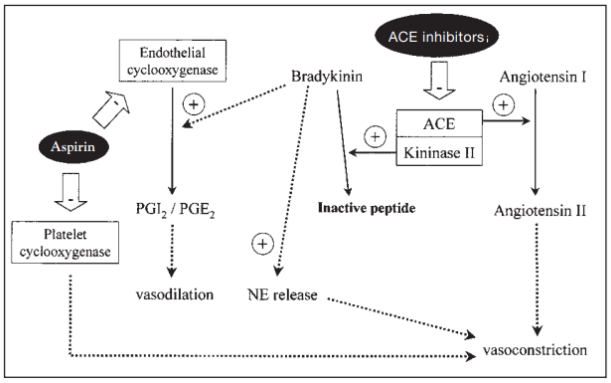

Figure 1: Interaction between Aspirin and Enalapril.

An alternative mode of interaction between an ACE inhibitor and aspirin is suggested by Levi et al [3] has conducted extensive research on factors that regulate norepinephrine release from sympathetic nerve endings in the heart. The authors reported that bradykinin increased the release of noradrenaline from the cardiac sympathetic nerves, whereas cyclooxygenase inhibition decreased this noradrenaline release [4]. In the affected heart, the secretion of vasoconstrictor from the endothelium is diminished, resulting in a predominant vasoconstrictor effect of norepinephrine. Increased norepinephrine release in stressful situations such as heart failure and myocardial ischemia can have an arrhythmia-inducing effect, leading to increased coronary vasoconstriction, which in turn can have a detrimental effect on cardiac function. ACE inhibitors affect this regimen in two ways. First, they help lower angiotensin II levels, thereby lowering circulating norepinephrine levels. However, they also increase the supply of bradykinin and continuously increase the heart's norepinephrine secretion (Figure 1). Aspirin can disrupt this process by inhibiting the cyclooxygenase enzyme and reducing its products. It has an additive effect on the release of norepinephrine via bradykinin. Therefore, it has been hypothesized that the addition of drugs that block cyclooxygenase enzymes to ACE inhibitor therapy may counteract the harmful effects of ACE inhibitors on norepinephrine secretion and provides additional benefits.

Conclusion

There is a theoretical possibility that a negative interaction between an ACE inhibitor and aspirin may reduce the beneficial effects of an ACE inhibitor in patients with coronary insufficiency.

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