AMP cíclico dilata vias aéreas. Olmesartana um antagonista do receptor 1 da angiotensina II aumenta expressão do AMPc e diminui a do TNF-alfa.

Seria a olmesartana indicada para asma?

cAMP regulation of airway smooth muscle Function.

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Source

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Abstract

Agonists activating β(2)-adrenoceptors (β(2)ARs) on airway smooth muscle (ASM) are the drug of choice for rescue from acute bronchoconstriction in patients with both asthma and chronic obstructive pulmonary disease (COPD). Moreover, the use of long-acting β-agonists combined with inhaled corticosteroids constitutes an important maintenance therapy for these diseases. β-Agonists are effective bronchodilators due primarily to their ability to antagonize ASM contraction. The presumed cellular mechanism of action involves the generation of intracellular cAMP, which in turn can activate the effector molecules cAMP-dependent protein kinase (PKA) and Epac. Other agents such as prostaglandin E(2) and phosphodiesterase inhibitors that also increase intracellular cAMP levels in ASM, can also antagonize ASM contraction, and inhibit other ASM functions including proliferation and migration. Therefore, β(2)ARs and cAMP are key players in combating the pathophysiology of airway narrowing and remodeling. However, limitations of β-agonist therapy due to drug tachyphylaxis related to β(2)AR desensitization, and recent findings regarding the manner in which β(2)ARs and cAMP signal, have raised new and interesting questions about these well-studied molecules. In this review we discuss current concepts regarding β(2)ARs and cAMP in the regulation of ASM cell functions and their therapeutic roles in asthma and COPD.

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Olmesartan Ameliorates Insulin Sensitivity by Modulating Tumor Necrosis Factor-α and Cyclic AMP in Skeletal Muscle

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Abstract

We have reported that tumor necrosis factor (TNF)-α in skeletal muscle is one of the determinants of insulin resistance and that the renin-angiotensin system may be related to the regulation of TNF-α in skeletal muscle. Recent studies have suggested the involvement of cyclic adenosine monophosphate (cAMP) in the regulation of TNF-α in vascular smooth muscle cells or monocytes. The aim of this study was to determine the relationship between cAMP and TNF-α in skeletal muscle in connection with the renin-angiotensin system. Six-week-old male Sprague-Dawley rats were fed either normal rat chow or fructose-rich chow for 6 weeks. For the last 2 weeks of a 6-week period, the rats were treated with a vehicle or with an angiotensin II type 1 receptor antagonist (olmesartan medoxomil, 0.1 mg/kg/day). TNF-α levels in the soleus muscle were significantly higher and cAMP levels in the soleus muscle were significantly lower in fructose-fed rats than in control rats. Olmesartan increased cAMP and reduced TNF-α simultaneously in fructose-fed rats. There was a significant negative correlation between levels of cAMP and TNF-α. Moreover, a cAMP analogue reduced TNF-α levels in the soleus muscle. These results indicate that the increase in TNF-α via suppression of cAMP may affect the induction of insulin resistance. In addition, the facts that olmesartan increased cAMP and decreased TNF-α suggest that a part of the TNF-α regulation by angiotensin II might consist of modulation of cAMP through Gi protein activation in skeletal muscle.