DRY COUGH AS AN ADVERSE DRUG REACTION DURING THE USE OF ANGIOTENSIN CONVERTING ENZYME INHIBITORS

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Annotation .

The most common adverse drug reaction due to the use of angiotensin-converting enzyme inhibitors is a dry cough due to the accumulation of bradykinin due to blockade of the angiotensin-converting enzyme, which is involved in its metabolism. The situation with the occurrence of dry cough requires a change in the drug (most often to angiotensin receptor blockers), because. a decrease in the dose of angiotensin-converting enzyme inhibitors reduces the antihypertensive effect of the therapy, while the appointment of effective doses of blockers angiotensin-converting enzyme neutralizes the effect of the renin-angiotensin-aldosterone system not by blocking the angiotensin-converting enzyme, but by acting on angiotensin II receptors, and as a result of this action, the metabolism of bradykinin does not change.

key words : angiotensin-converting enzyme , accumulation of bradykinin , dry cough .

Introduction

Mechanism of action of angiotensin-converting enzyme inhibitors:

Renin itself binds to α2-globulin, resulting in the formation of a weakly active decapeptide angiotensin II, which under the influence of angiotensin-converting enzyme is converted into an octapeptide angiotensin II. The latter has a pronounced vasoconstrictive effect, stimulates the secretion of aldosterone, promotes sodium reabsorption in the renal tubules and, as a result of an increase in plasma osmotic pressure, an increase in circulating blood volume. The effects of angiotensin-converting enzyme inhibitors also include increased resolution of bradykinin , which has a vasodilatory effect, participation in the metabolism of neuropeptides . Under normal conditions , the body's pressor systems (renin-angiotensin-aldosterone and sympathoadrenal) and depressor systems (kallikrein-kinin with bradykinin as a leading role) counteract each other and are in dynamic balance, exerting vasoconstrictive and vasodilating effects, respectively. In diseases (hypertension, chronic heart failure), the predominance shifts towards the pressor system. It should be noted that the angiotensin-converting enzyme is involved in the regulation of both systems. Angiotensin-converting enzyme is found both in the blood serum (plasma link of the renin-angiotensin-aldosterone system), and in endothelial, nervous tissues, myocardium, epithelium of the renal tubules, seminal appendages (the so-called tissue link of the renin-angiotensin-aldosterone system). The plasma link is activated quickly, but has a short-term effect, while the tissue link, on the contrary, is realized gradually, but persists for a longer time. The ratio of plasma and tissue units of the renin-angiotensin-aldosterone system is approximately 1:9. Angiotensin II, which is formed as a result of the activities of the plasma and tissue links of the renin-angiotensin-aldosterone system, has a vasodilating effect through several mechanisms:

1. Direct effect on angiotensin receptors ;
2. Increased secretion of norepinephrine from sympathetic nerve endings;
3. Increased secretion of endothelin I, a potent vasodilator, by endothelial cells;
4. Increased entry of free calcium into the cell.

tissue link of the renin-angiotensin-aldosterone system is responsible for the development of lesions of internal organs: myocardial angiotensin II activates proto-oncogenes , stimulates hypertrophy and fibrosis of muscle fibers. These events are also observed in the smooth muscles of peripheral vessels. Angiotensin-converting enzyme inhibitors prevent the multiple vasoconstrictive effect of angiotensin II, cause an increase in plasma renin concentration and a decrease in that of angiotensin II, prevent the destruction of bradykinin , and reduce the synthesis and secretion of aldosterone. The consequence of the action of angiotensin-converting enzyme inhibitors is the weakening of the vasoconstrictor, antidiuretic and antinatriaemic effects of angiotensin II. On the contrary, there is an increase in the vasoconstrictor and natriuretic effects of bradykinin .

Mechanism of action of angiotensin II receptor blockers :

Angiotensin II directly acts through special receptors that are located in the wall of blood vessels, nerve endings (types I and II). The physiological action of angiotensin II, manifested through type I receptors, leads to vasodilation, increased sodium reabsorption in the renal tubules, intestines, aldosterone release, remodeling of the vascular wall and myocardium, activation of the sympathoadrenal system (both central and peripheral), water retention in the body renin release. The listed effects of angiotensin II regulate blood pressure, maintain it at a high level in hypertension. Blockade of type I receptors makes it possible to achieve the elimination of pathological hypertonicity of the vascular wall in arterial hypertension and the prevention of its and myocardial pathological remodeling . There is also a regression of myocardial hypertrophy, improvement of its diastolic function. As for type II receptors for angiotensin II, located in the tissues of the brain, myocardium, adrenal medulla, kidneys, uterus and ovaries, the beneficial effects of angiotensin II are realized due to them : stimulation of nitric oxide synthesis, natriuretic effect, antiproliferative effect. In relation to the cardiovascular system, the effects realized through type II angiotensin receptors are also favorable, but are much less pronounced than those realized through type I

receptors: there is some vasodilation, an antiproliferative effect in relation to endothelial cells and the muscular layer of the vascular wall , inhibition of myocardial hypertrophy.

Purpose of the study :

1. Find out the prevalence of dry cough as a side effect of taking angiotensin-converting enzyme inhibitors.
2. Find out if this reaction is observed further in such patients after switching the drug to an angiotensin II receptor blocker .

Materials and research methods :

We studied the medical records of 43 patients aged 40 to 59 years, taking angiotensin-converting enzyme inhibitors for one reason or another (hypertension, chronic heart failure). The prevalence of dry cough as an undesirable drug reaction was assessed both during the use of angiotensin-converting enzyme inhibitors and after switching the drug to an angiotensin II receptor blocker .

Research results :

1. Dry cough as an undesirable drug reaction of taking angiotensin-converting enzyme inhibitors was observed in 5 people (patients did not notice dry cough before);
2. In these patients, the drug was switched to an angiotensin II receptor blocker , after which, after 2-4 weeks, none of the patients noted a dry cough.

Conclusion :

Angiotensin-converting enzyme inhibitors have a relatively small number of adverse drug reactions, and dry cough, as the most common of them, can significantly reduce the standard of living of patients, and in some cases (for example, in chronic obstructive pulmonary disease) cause a worsening of the disease. Changing the drug to an angiotensin II receptor blocker , comparable in effectiveness to angiotensin-converting enzyme inhibitors, eliminates dry cough as

an undesirable drug reaction without reducing the effectiveness of antihypertensive therapy.

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