ANGIOTENSIN-CONVERTING ENZYME INHIBITOR LISINOPRIL: FEATURES OF USE IN CARDIOLOGY

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Abstract. The renin-angiotensin system plays an important role in the development of cardiovascular diseases. Over the past decade, numerous studies have been conducted that have examined the clinical effectiveness of angiotensin-converting enzyme (ACE) inhibitors in various clinical conditions.

Keywords: ACE, cardiology, effectiveness, enzyme, disease.

INTRODUCTION

ACE inhibitors (according to currently available data) are generally not superior to other classes of antihypertensive drugs in terms of their effect on the prognosis of arterial hypertension (AH). However, the advantage of ACE inhibitors as first-line drugs for hypertension can be considered in patients with concomitant heart failure, left ventricular systolic dysfunction or diabetes mellitus, previous myocardial infarction or stroke, as well as in patients at high risk of coronary disease. The effectiveness of drugs in this group in these samples was confirmed in special studies [1–3].

MATERIALS AND METHODS

Recently, data have appeared on the possibility of a beneficial effect of ACE inhibitors on the prognosis of life of patients with uncomplicated ischemic heart disease (HOPE, EUROPA studies), in connection with which the issue of including this group of drugs in the mandatory list of drugs prescribed was decided - for this disease (along with aspirin, β-blockers and statins).

RESULTS AND DISCUSSION

The group of ACE inhibitors is quite large. These drugs differ from each other in the following parameters:

• chemical structure (presence or

the absence of a sulfhydryl group, some other structural features of the molecule);

• metabolic features (whether the drug is metabolized or not metabolized during the first passage through the liver);

• peculiarities of drug excretion from the body (only by the kidneys or both the kidneys and the liver);

• tissue specificity;

• duration of action. The presence of a large number of ACE inhibitors poses a difficult task for clinicians in choosing a specific drug for a specific patient. The question arises to what extent the above-mentioned differences between ACE inhibitors affect their clinical effectiveness and whether these differences should determine the choice of a particular drug. The answer to this question is generally negative, primarily because today there is no reason to believe that these particular features determine the clinical effectiveness of a particular drug from the group of ACE inhibitors.

Since, as noted above, the main effect of ACE inhibitors is their ability to improve the prognosis of diseases, it is fundamentally important whether this ability is inherent to the same extent in all drugs in this group. Please note that the evidence base regarding the effect of a particular ACE inhibitor on disease outcomes varies greatly for different drugs. This raises the question of how far the effects proven for one drug can be attributed to another drug from the same group (this question actually arises when considering other groups of drugs, not just ACE inhibitors), in other words, how universal is the concept of “class effect”.

C. Furberg, in a number of publications devoted to this issue [4, 5], comes to the unequivocal conclusion that in no case can the effect of improving patient survival achieved by using one drug be transferred to another a drug of the same

class (it proves this in different groups of drugs, in particular statins). In relation to ACE inhibitors, this idea can be illustrated, for example, by the fact that not all ACE inhibitors have proven their effectiveness in the treatment of patients with uncomplicated ischemic heart disease: while ramipril and perindopril significantly improved the prognosis of this disease (HOPE and EUROPA studies), quinapril did not have such an effect (QUIET study) [2]. According to C. Furberg, only a few ACE inhibitors today can be considered drugs with proven effects (he includes 5 drugs: captopril, enalapril, lisinopril, ramipril, trandolapril); It is these drugs that should be given preference in real clinical practice (at least for those diseases for which the effectiveness of specific drugs from this group has been proven).

Lisinopril, unlike many ACE inhibitors, is not a prodrug and is not metabolized in the liver; it is excreted unchanged by the kidneys. The half-life is about 12 hours (increases significantly with impaired renal function). Lisinopril has low tissue specificity, being significantly inferior in this regard to such drugs as quinapril, benazepril, ramipril, perindopril. A typical side effect for ACE inhibitors—dry cough—is observed much less frequently when taking lisinopril (1.6%) than when taking captopril, perindopril and enalapril (5.1; 2.2 and 7% respectively) [3]. This may be due to the low lipophilic properties of lisinopril, which affect the accumulation of the drug in tissues. Like all ACE inhibitors, lisinopril is a metabolically neutral drug. Despite its unremarkable pharmacological properties, lisinopril is one of the most popular ACE inhibitors, primarily due to the fact that it has been used quite actively in large controlled studies.

Lisinopril was one of the first ACE inhibitors, which was proven to improve the prognosis of life in patients with acute myocardial infarction. The GISSI-3 study (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico) on more than 19,000 patients showed that the administration of lisinopril starting from the first day of acute myocardial infarction for 6 weeks (initial dose 5 mg per day, then 10 mg per day) contributed to a statistically significant reduction in

overall mortality both compared with the control group and compared with the group receiving transdermal nitroglycerin (hazard ratio 0.88; 95 % confidence interval 0.79–0.99), as well as a significant improvement in left ventricular function. This difference persisted after 6 months. The positive effect of lisinopril on the outcome of the disease was also revealed in a subgroup of elderly patients. The incidence of recurrent myocardial infarction, post-infarction angina, cardiogenic shock and stroke did not differ between the lisinopril and placebo groups [3].

The ATLAS (The Assessment of Treatment with Lisinopril and Survival) study is very important from the point of view of using evidence-based medicine data in real clinical practice [4]. This double-blind, randomized study included 3164 patients with heart failure of NYHA functional classes II–IV. All patients were randomly assigned to two groups: those receiving lisinopril in low doses (2.5–5 mg per day) and those receiving lisinopril in high doses (32.5–35 mg per day). These doses, according to preliminary data, corresponded to the doses of other ACE inhibitors that contributed to a significant reduction in mortality in heart failure. The duration of observation was 39–58 months.

In fact, the ATLAS study compared ACE inhibitor therapy, which is recommended based on the results of controlled studies, with therapy with the same drugs, which is most often actually prescribed to patients (it is well known that ACE inhibitors are used in everyday clinical practice in patients with heart failure). usually prescribed in minimal doses [12]) to prevent severe hypotension.

Although there was no significant difference in overall mortality between groups in the ATLAS study (mortality difference was 8% in favor of patients treated with high doses, $p = 0.128$), treatment with high doses significantly reduced the risk death and hospitalization from any cause (by 12% compared with the use of low doses, $p = 0.002$), as well as the risk of death and hospitalization due to cardiovascular diseases (by 9%, $p = 0.027$). It is interesting that clinical

improvement (dynamics of the class of heart failure) was expressed approximately equally in the groups treated with low and high doses of lisinopril.

CONCLUSION

Currently, the ACE inhibitor lisinopril is a well-studied drug that has been used in a number of large controlled studies and has proven its effectiveness in chronic heart failure, acute myocardial infarction (starting from the first day), complicated by impaired left ventricular function, as well as with hypertension. Of course, this drug should be prescribed exactly as it was done in the above-mentioned studies, and only then can the doctor expect to obtain the same results in terms of improving the prognosis of the disease.

REFERENCES

1. Adasheva T.V. and others // Rus. honey. magazine 2013. T. 11. No. 2. P. 62.

2. Andrushchishina T.B. and others // Rus. honey. magazine 2012. T. 10. No. 10. P. 472.

3. Gorokhova S.G. // High-quality clinical practice. 2013. No. 2. P. 65.

4. Petrov V.I. and others // Medicinal Bulletin. 2015. No. 3. P. 14.